Vol. IV. No. 3. Serial No. 15. OCT 22 1920 *July-September, 1920*

ENDOCRINOLOGY

The BULLETIN of the ASSOCIATION for the STUDY of

INTERNAL SECRETIONS

CONTENTS

Published Quarterly by the Association for the Study of Internal Secretions, 1100-1103 Title Insurance Bldg., Los Angeles, California. Subscription Rates: $5.00 a Year in Advance. Single Copies $1.50, Postpaid.

Entered as second-class matter February 5, 1917, at the post office at Los Angeles, California, under the Act of March 3, 1879.

Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized September 17, 1920.

ACCEPTED

"The Journal" A. M. A.
August 7, 1920.

As Conforming to the Rules

of

The Council on Pharmacy and Chemistry,
A. M. A.

Ovarian Residue Tablets, H. W. & D.

50 Tablets in a Tube

"That under present conditions of preparation ovarian residue is in general superior in its clinical results to the commercial articles now on the market."

Sterile Solution of Lutein, H. W. & D.

(Corpus Luteum)

In Ampules for Intramuscular Injection

6 Ampules in a Box

"With many misgivings as to success, I tried corpus luteum extract intramuscularly by hypodermic with gratifying results, as the following cases will show."

NOTE—Reprints of papers by prominent gynecologists from which the above quotations are made and bearing on these remedies sent upon request.

Hynson, Westcott & Dunning

BALTIMORE, MARYLAND

ENDOCRINOLOGY

THE BULLETIN of the ASSOCIATION

for the STUDY of

INTERNAL SECRETIONS

JULY-SEPTEMBER, 1920

CLASSIFICATION OF DISORDERS OF THE HYPOPHYSIS*

Wm. Engelbach, M. D.

St. Louis

To have the opportunity of submitting a classification of the disorders of the hypophysis to this audience, many of whom have done original work upon this gland, is indeed a privilege. This presentation is made with the view that the many complexities encountered in correlating the clinical manifestations of these disorders, with the changes in function and histology of the hypophysis, will be clarified by its discussion. The primary essentials relative to the physiology of the pituitary body, upon which this classification is based, have been deduced almost entirely from the theoretical conclusions of pituitary function advanced by American investigators (Cushing, Goetsch, Homans, Crowe, and Bab). The application of these principles has been stimulated by our analysis† of 892 endocrine cases, of which 147 were diagnosed disorders of the pituitary gland; 350, of the thyroid; 194, of the gonads; 186, pluriglandular disorders; 10, diseases of the adrenals and 5, thymus diseases. Of the 123 hypopituitary disorders, 23 were grouped as anterior lobe; 3, as pos-

*Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

†From observations made in conjunction with Dr. J. L. Tierney, to whom we are indebted for the determinations on basal metabolism and carbohydrate tolerance.

terior lobe; and 86, as bilobar insufficiencies. The hyperpituitarisms totaled 24, of which 6 were anterior lobe; 2, posterior lobe, and 16, bilobar varieties. There were 11 cases of diabetes insipidus, or hypophyseal polyuria, some of which were associated with an anterior lobe or a pars nervosa syndrome. Pituitarism as a part of a pluriglandular complex (not included in the 147 primary pituitary disorders) occurred in 122, making a total of 269 cases in which clinical manifestations of pituitarism were present. Of the total number of pituitary cases, only 8, or 6 per cent, were neoplastic in origin. Conclusions, dependent upon the differentiation of the clinical manifestions determined from comparing pituitary with other endocrine disorders, have substantiated to a considerable degree the theories of the functions of the individual lobes of the pituitary gland.

Lobar Grouping. This classification separates the hypophysis into two lobes, the anterior and the posterior, with the pars intermedia as part of the latter. The clinical manifestations, due to abnormal secretions of one or both of these lobes, are taken as the chief guide for the grouping of the disorders. The clinical syndromes (exclusive of pituitary neighborhood signs and symptoms), formerly termed "glandular" symptoms, are named "hormonic" signs and symptoms, a qualification applying to all endocrine disorders. The "hormonic" signs and symptoms are defined as physical or metabolic changes associated with other endocrine symptoms due to an abnormal secretion of a ductless gland. Those pertaining to the pituitary disorders are divided into the physical, metabolic, and other endocrine symptoms. The physical "hormonic" signs are subdivided into the general and regional.

Among the general "hormonic" signs are the well-known changes in osseous development, producing classical disproportion in the measurements (torso, lower measurement, and span), unusual development of the voluntary musculature, abnormal contraction of the unstriped muscle tissue, pigmentation, and hair distribution. Among the significant regional "hormonic" signs are local changes in the head, nose, teeth, chin, hands, and genitalia, localized adiposity, pigmentation, etc. Other important pituitary endocrine symptoms are polyuria, changes in basal metabolism, carbohydrate tolerance, mentality, other endocrine secretions, temperature, pulse, and blood-pressure.

Certain combinations of the above "hormonic" signs and symptoms are taken as indicative of abnormal secretion of an individual lobe or of both lobes of the pituitary gland. These combinations or clinical syndromes were present so constantly in classical types and varieties of pituitary disorders, that they have been deemed the most valuable as a grouping system for these diseases. The neighborhood signs and symptoms, while important as diagnostic evidence of the neoplastic varieties of the disorders, were of little value for differentiating the varieties and types for the purpose of classification or diagnosis. This is true on account of the fact that pituitary tumors were found associated with all the various clinical syndromes. Furthermore, the incidence of pituitary tumor was so rare (6 per cent of the cases herewith reported) that its symptomatology was practically useless as a basis for general classification. The histopathology of the hypophysis, particularly of the a-neoplastic type, has been too poorly defined to make it a dependable basis worthy of classification.

Functions of the Lobes of the Hypophysis. In order to justify this lobar classification of these disorders, it becomes necessary to establish the function of each lobe of this gland producing these specific "hormonic" signs and symptoms. As the function of the entire pituitary body, as well as of its individual lobes, is yet a matter of controversy, this will be difficult and must remain somewhat questionable. In attempting to assign definite "hormonic" syndromes to specific disturbances in the lobes of the hypophysis, the writer has accepted, to a large extent, the early experimental work of Cushing, Goetsch, and others. Personal clinical observations, so far made upon these hormonic complexes, have seemed to substantiate their theories, in contradiction to those of Bell, Falta, Fisher, Biedl, and others.

As will be seen from the following table, the *major hormonic signs of the anterior lobe* (A and B) are those referable to the growth and function of the *osseous* and *genital* systems, and the minor signs (C, D, E, F, G and H), to the dermal system, mentality, temperature, pulse and blood-pressure. The major signs attributed to the posterior lobe (I, II, III and IV) are those resulting in disturbed metabolism, deposition of adipose tissue, polyuria and unstriped muscle contraction. Associated

TAB

HORMONIC SIGNS OF THE ANTE

	HYPOPITUITARISM	
	Preadolescent	**Post**adolescent
A. **Osseous**	A. **Undergrowth. All Bones LORAIN-LEVI** type	A. **Undergrowth. Short and flat bones** only. (Normal long bones)
1. Stature a. Measurements	1. Short a. Torso greater than lower. Span less than height	1. Tall, or normal a. Varies. Torso greater than lower or less than lower (eunuchoid)
2. Head a. Sinuses b. Nose	2. Small a. Small b. Pointed, straight	2. Small a. Small b. Pointed, straight
c. Superior Maxilla	c. Normal	c. Normal
d. Chin	d. Pointed, sharp	d. Pointed, sharp
e. Sella Turcica (X-ray)	e. Small, except **neoplastic** type enlarged	e. Small, except **neoplastic** type enlarged
3. Hands	3. Type "en petit," one-third smaller than normal	3. Small
a. Phalanges (X-ray)	a. Narrow, tapering, tuberosities and tufting absent	a. Narrow, tapering tuberosities and tufting absent
4. Pelvis a. Genu	4. Broad, feminine type a. Valgum	4. Broad, feminine type a. Valgum
B. **Genital**	B.	B.
1. Gonads (ovary or testicle)	1. Infantile	1. Normal
2. Uterus	2. Infantile	2. Normal
3. Menses	3. Amenorrhea, metrorrhagia, and dysmenorrhea	3. Tendency to dysmenorrhea, amenorrhea, and metrorrhagia
4. Sterility and Impotence	4. Present	4. Present
5. **Secondary Sex Characters**	5. Absent	5. Present
C. **Muscular**	C. Proportionate to development	C. Normal
1. Muscle Tonus	1. Normal	1. Fatiguability frequent
D. **Mental**	D. Usually deficient or retarded	D. Average
E. **Dermal** a. Teeth b. Hair Distribution	a. Upper incisors enlarged, lateral occlusion good b. Absent	a. Occasional separation and frequent enlargement of upper incisors b. Normal
F. **Temperature**	F. Subnormal	F. Subnormal
G. **Pulse**	G. Slow	G. Slow
H. **Blood-pressure**	H. Hypotension, or normal	H. Hypotension, or normal

LE I
RIOR LOBE OF THE HYPOPHYSIS

HYPERPITUITARISM

Preadolescent	**Post**adolescent
A. **Overgrowth of all bones** (Normal giant, Eunuchoid giant, Acromegalic giant) — **Gigantism**	A. **Overgrowth. Acral, short and flat bones** only. (Long bones short) **Acromegaly**
1. Abnormally tall	1. Short and stocky, or normal
a. Normal giant: torso = lower, span = height Eunuchoid giant: torso less than lower, span greater than height Acromegalic giant: torso greater than lower, span less than height	a. Acromegaly: torso greater than lower, span less than height
2. Large	2. Large
a. Large	a. Large
b. Pointed, normal (eunuchoid giant) Blunt (acromegalic giant)	b. Blunt, rounded
c. Normal, except prominent in acromegalic giant	c. Prominent
d. Pointed, except prognathism in acromegalic giant	d. Rounded, blunt. Prognathism
e. Normal, except **neoplastic** type enlarged	e. Normal, except **neoplastic** type enlarged
3. Type "en longe," one-third larger than normal. No disproportion	3. Type "en large," spade hand, wrist wide, fingers broad and clubbed. Infiltration of soft tissues over bones. Hands and head involved
a. Wide, dense, tuberosities large, terminal tufting, exosteses	a. Wide, dense, tuberosities large, terminal tufting, exostoses
4. Narrow, masculine type	4. Narrow, masculine type
a. Varum	a. Varum
B.	B.
1. Large, well developed	1. Large, well developed
2. Normal	2. Normal
3. Normal	3. Normal
4. Absent (present in a few years with transition to hypoactivity)	4. Absent (present after many years with transition to hypoactivity)
5. Present (even after hypoactivity occurs)	5. Present (even after hypoactivity occurs)
C. Normal, or overdeveloped	C. Overdeveloped
1. Loss after few years' overactivity)	1. Retained after age of 40-45
D. Apathetic (after activity changes)	D. Abnormally developed, temperamental, loquacious, unstable
a. Enlarged and separated upper incisors. Lowers separated in acromegalic giant	a. Separation of upper incisors constantly; frequently of lower, with prognathism
b. Increase on torso	b. Marked increase on extremities and chest
F. Normal	F. Normal
G. Normal	G. Normal
H. Normal. Hypotension after change to hypoactivity	H. Normal, or above normal

with these are minor signs, affecting the secretion of other endocrine glands, the nervous system, temperature and pulse.

While it is true that the secretion from the anterior lobe seems to have a definite effect upon the development and function of the osseous and genital systems, it is acknowledged that other factors, endocrinous and endogenous, undoubtedly have considerable influence upon both the growth and development of these two systems. Not all cases of retarded osseous growth and aplasia, for instance, can be attributed to hyposecretion of this lobe of the hypophysis. The French school (Brissaud, Meige, Bauer, Anton and Brammel) have many subdivisions of infantilism (''nanisme,'' ''chetivisme,'' ''nanisme complet''), many types of which have no relation to pituitary disorders. The above table contrasts the hormonic signs related to the anterior lobe in hypopituitarism with those of hyperpituitarism, and demonstrates the differences dependent upon the age at which this disturbed activity occurs (pre- and post-adolescent). Attention is directed particularly to the extreme opposite change noted in the osseous system in pre-adolescent hypopituitarism (first column) as compared with pre-adolescent hyperpituitarism (third column).

The effect of the secretion from the anterior lobe upon the muscular tonus is a subject which has received comparatively little attention, but which has appeared to the writer as being almost as important as the difference present in the osseous growth and development. This is particularly striking when one compares the muscular development and tone of pre-adolescent hypopituitarism (Lorain-Levi type) with those of post-adolescent hyperpituitarism (acromegaly). The extreme difference in the genital function and development is also emphasized in comparing the foregoing two types. In the first (Lorain-Levi type) the genitals are infantile and functionless, with the presence of sterility and impotence; whereas in the acromegalic, the genitals are unusually well developed and associated with hypersexuality. In pre-adolescent varieties of both over- and underactivity of this lobe, there is a tendency to decreased genital function. This is present as a cardinal sign in the hypopituitary post-adolescent subject, and is soon acquired in pre-adolescent hyperpituitarism, on account of the early transition to inactivity in this variety. Decreased genital function and muscle tonus

occurred so constantly with hypoactivity of the anterior lobe, that they established themselves as the best indicators of the state of activity of this lobe. Hence, the genital functions (menses, libido, and potency) and the muscular tonus (muscle fatigue or physical capacity), taken with the temperature, pulse, and blood-pressure, were considered, at the time of their determination, the significant signs of activity. The osseous changes, genital development, and secondary sex characters were interpreted as evidence of former activity which might have changed to the opposite state.

The intermittent enlargement and infiltration of local parts, such as the hands and face, in acromegaly, were undoubtedly due to changes in the soft tissue covering the short and flat bones involved, and not a result of osseous change. The rapid changes in these localized swellings, besides the frequently associated sweating of these parts, helped to prove this origin. While there was no nervous syndrome specific of pituitary disorder, the different mental states, as described above, were most frequently demonstrable. The most significant mental change was probably that occurring in gigantism and acromegaly, with change of activity in this lobe. Change from a hypermental state to one of depression, apathy and indifference, if associated with loss of genital function and muscle tone, was considered particularly significant of transition to hypoactivity. The orthodontial markings in anterior lobe insufficiencies varied considerably. In the pre-adolescent hypopituitary individual, there was usually a tendency to overcrowding of the lower teeth, with fairly good lateral occlusion of the upper. The frontal incisors were constantly enlarged in those cases in which there was absence of genital function and development. The separation of the upper incisors occurred in post-adolescent hypopituitarism, and was usually present in pre- and post-adolescent hyperpituitarism; whereas the separation of the lower teeth was limited to the acromegalic giant and acromegaly, being absent in other hyperpituitarisms, as well as in all deficient secretions of the anterior lobe. The blood-pressure, temperature, and pulse were important signs of activity in this, as well as in other endocrine glands, but were by no means specific for pituitarism. Hence, they are valuable as signs of activity, but not as signs of any individual ductless gland. They are respectively subnormal and slow in the

hypoactive cases, and normal or slightly above normal in the opposite state of secretion.

Basal metabolism determinations* have been made on only 32 of the cases which came under observation during the last six months. These cases have been grouped among the five varieties, so that there were too few in any one variety from which to draw satisfactory conclusions.

The basal metabolism in these few cases of disorders of the anterior lobe of the hypophysis varied considerably. This is in contradiction to the theories previously advanced, to the effect that the anterior lobe secretion has no influence upon metabolism. One would believe that either there must be some relationship between the metabolism and the function of this lobe, or the clinical diagnosis excluding the posterior lobe of the hypophysis and the other endocrine glands, as an accompaniment in these cases, was incorrect. In the simple anterior lobe dyscrasias reported herewith, 7 cases had a basal metabolism varying from the normal. In 5 cases it was decreased, varying from 2 to 30 per cent, and in 2, it was increased 14 and 15 per cent respectively. In one case in which anterior lobe extract was given therapeutically, the basal metabolism was increased from —30 to +8 per cent during six weeks' treatment. This increase in metabolism to slightly above the normal was accompanied by relief of other symptoms, such as headaches, mental disability, muscular fatigue, loss of libido, etc. In the pure hyperactivities of the anterior lobe, the same discrepancy in basal metabolism determinations occurred. In the 4 cases in which the metabolism was determined, it was found normal in 2, and increased in 2. In 5 cases originally diagnosed as simple anterior lobe hypoactivities, it was found that the basal metabolism was increased beyond 10 per cent, and the sugar tolerance markedly decreased,

*Benedict's Portable Apparatus No. 19 was used for these determinations. The linear formula of D. Du Bois and E. F. Du Bois was used for computation of the area of body surface. The following table of Aub and E. F. Du Bois was taken as the normal standard for the calories per square meter of body surface per hour:

(Height-Weight Formula)

Age, Years	Males	Females
14-16	46.0	43.0
16-18	43.0	40.0
18-20	41.0	38.0
20-30	39.5	37.0
30-40	39.5	36.5
40-50	38.5	36.0
50-60	37.5	35.0
60-70	36.5	34.0
70-80	35.5	33.0

which necessitated a change in the diagnosis and grouping to the bilobar division, under the heteroactive variety.

The *carbohydrate tolerance** was estimated in 10 cases of anterior lobe dyscrasia. Of these, 7 were decreased, and 3 were increased in activity. Of the hypopituitarism cases, 5 showed an increased, and 2, a decreased sugar tolerance; whereas, in the hyperactivities, 2 cases showed an increased, and 1, a decreased tolerance. In the 2 cases having an increased basal metabolism, the sugar tolerance curve was normal.

The hormonic signs due to increased and decreased activity of the posterior lobe are given in detail below. It will only be necessary to refer to the fact that they are exactly opposite, a statement that cannot be proved absolutely on account of the considerable difference of opinion regarding the functional effects of this lobe, as related to specific influence upon other processes and structures of the body. It will be observed that the writer is of the opinion that this lobe of the hypophysis has practically no relation to the growth or function of the osseous and genital systems. On the contrary, its function is limited directly to the regulation of the metabolism, and indirectly to effects upon other organs and tissues which deal with metabolic procedure.

The influence of the secretion of the posterior lobe upon metabolism, estimated from personal observations based upon the determination of basal metabolism and carbohydrate tolerance, was found more definite in its relationship than those changes of metabolism associated with the simple anterior lobe dyscrasias. The following is a summary report of the basal metabolism and carbohydrate tolerance determinations made upon cases of pituitary disorder in which the posterior lobe was involved independently, or was associated with an anterior lobe syndrome. Many of the cases having anterior lobe disorder had a secondary gonad disturbance, but none was of the pluriglandular syndrome having hormonic signs of the thyroid, adrenals, or other ductless glands. The *basal metabolism* determi-

*The sugar tolerance was estimated by the Janney-Isaacson method. The blood sugar was estimated first after 15 hours' fasting. Glucose, 1.59 grams per kilogram of body weight, was given, and blood sugar estimations were again made, one hour and two hours following the ingestion of this amount. A normal curve was arbitrarily established, as follows: after 15 hours' fasting, 0.10; after the first hour, 0.18; and after the second hour, 0.15. A decreased tolerance was considered one which would produce a higher curve during the two hours' estimations than the normal curve. Increased tolerance would show a curve 3 or 5 points below this curve.

TABLE II

HORMONIC SIGNS OF THE **POSTERIOR** LOBE OF THE HYPOPHYSIS

	HYPOPITUITARISM	**HYPER**PITUITARISM
I. **Metabolism**	I.	I.
a. Basal Metabolism	a. Decreased	a. Increased
b. Carbohydrate Tolerance	b. Increased	b. Decreased
c. Glycosuria and Hyperglycemia	c. Absent	c. Present
II. **Adiposity**	II. Marked girdle, mons and mammary	II. Absent, usually emaciation
III. **Polyuria**	III. Present (Pars Intermedia?)	III. Absent (or present with glycosuria)
IV. **Involuntary Muscle Contraction**	IV.	IV.
a. Intestinal	a. Absent; frequent intestinal atony	a. Present; frequent intestinal spasticity
b. Uterine	b. Absent	b. Present
V. **Endocrine Secretion**	V.	V.
a. Thyroid	a. Hypoactivity (hibernation)	a. Hyperactivity
b. Adrenals	b. Insufficiency?	b. Hyperactivity?
c. Gonads	c. Hypoactivity (with Anterior Lobe disorder)	c. Hyperactivity (with Anterior Lobe disorder)
d. Pancreas	d. Normal (increased sugar tolerance)	d. Hypoactivity (decreased sugar tolerance)
VI. **Nervous**	VI. Apathy; Somnolence frequent	VI. Psychic instability
VII. **Temperature**	VII. Subnormal	VII. Normal
VIII. **Pulse**	VIII. Slow	VIII. Rapid

nations were made in 18 cases in which the posterior lobe was involved. Of these, 14 cases were hypoactivities, and 4, hyperactivities. In the hypoactivities, this metabolism was decreased in 5 cases, normal in 5 cases, and increased in 4 cases. Of the 4 cases showing an increased metabolism, against the rule for hypoactivities of this lobe, it occurred in 2 after treatment, and in 1 associated with a polyuria. This practically left only 1 case which had an increase in metabolism, not conforming to the supposition that decreased secretion of this lobe is constantly associated with decreased metabolism. Of the 4 hyperpituitarisms, the metabolism was increased in 2, and normal in 2, all fitting perfectly into the clinical diagnosis.

In 61 cases diagnosed as posterior lobe disorders, the *carbohydrate tolerance* was determined. Of these 61, 3 were grouped with the hyperactive variety, in 2 of which the sugar tolerance was increased, and in 1, decreased. In 58 cases a diagnosis was made of hypoactivity of this lobe, which showed in 53, an increased, and in 5, a decreased sugar tolerance. A recent contribution by Rohdenburg, Bernhard and Krehbiel, upon the study of the sugar mobilization, based upon 228 cases (cancer, tuberculosis, thrombo-angiitis, cirrhosis of the liver, myocarditis, etc.), discredits to a considerable extent the value of the carbohydrate tolerance test in metabolic disturbances. They conclude that in other conditions, as widely different as diabetes, tuberculosis, epithelioma, and pregnancy, a blood sugar curve is found, similar to that in metabolic disturbances; that many of these conditions are accompanied by hyperglycemia and that concentration of the blood sugar is not the sole factor concerned in the development of glycosuria.

The classical obesity interpreted as a "hormonic" sign of posterior lobe hypopituitarism, consists of girdle- and mons-adiposity, to which, in some cases, is added mammary adiposity. There is yet considerable controversy concerning the cause of this obesity. Its character and location have suggested secondary gonad insufficiency as its origin, because this frequently accompanies the bilobar cases having anterior lobe insufficiency. An argument against this cause of the obesity is that it is absent in the pure anterior lobe insufficiency in which there is complete aplasia and absence of function of the gonads. The writer has observed cases of this kind, in the female, aged 36 and 38 years,

in which there was complete amenorrhea and infantilism of the genitalia during the entire life, without the development of this typical adiposity. The emaciation which is present in hypersecretion of this lobe is easily accounted for on the basis of increased metabolism. The rapid loss of weight and emaciation frequently accompanying hypophyseal polyuria, however, is more difficult to explain, particularly if this polyuria is attributed to decreased secretion of the posterior lobe. If both these functions (polyuria and adiposity) are attributed to hyposecretion of the posterior lobe, then we should obtain adiposity much more frequently with the diabetes insipidus syndrome, which clinical experience demonstrates is more constantly associated with emaciation. Biedl has reported some exceptional cases, however, in which this peculiar combination of adiposity and polyuria occurred. It is not uncommon to have a history of early transient polyuria, followed later by adiposity, which might be due to a change of activity of this lobe. Bab's theory that the polyuria is due to *hypo*secretion of the pars intermedia, not including the pars nervosa, seems to approach nearer to an explanation of the clinical combinations, as well as the therapeutic relief which many of these cases obtained from hypophyseal treatment. The argument that this polyuria is really due to hypersecretion, on account of the fact that it is associated with so many other symptoms of posterior lobe hypersecretion, such as increased metabolism, decreased sugar tolerance, hypophyseal glycosuria, emaciation, and bladder and intestinal tenesmus, has not been entirely disproved.

The control of the contraction of the unstriped muscles, particularly those of the intestine and uterus, as well as of the bladder and the vascular and bronchial systems, is one of the most striking and easily demonstrable effects of the secretion of the posterior lobe. The writer has used the constriction effect of this substance upon the intestinal muscle ("intestinal reaction") to define the tolerable dose of pituitary extracts in the treatment of posterior lobe insufficiency. Extracts of the posterior lobe are given in dosage to the amount producing definite intestinal cramps, followed by evacuation. This reaction occurs within ten or fifteen minutes after giving this substance hypodermically. The dosage at which this reaction occurs is taken as the normal physiologic dose, and increase above this amount for

therapy is deemed inadvisable. If a larger dose is given, that which is described as a "general reaction" occurs. This consists of tremor, tachycardia, and emotionalism. The effect of extracts of this lobe upon the nervous system is strikingly demonstrated by giving so intolerable and untoward a dose. Mental symptoms from so large an injection, consisting of emotional attacks, crying, laughing, shouting ,and, in some, definite brainstorm, simulating temporary insanity and obsessions, have been produced. The "intestinal reaction" was tested out by the writer for its diagnostic value to determine whether the amount of extract producing these intestinal symptoms might not indicate to some degree the sufficiency of the posterior lobe. It was thought originally that cases having a deficient secretion from this lobe, would require a much larger injection to produce the "intestinal reaction" than those having a normal or increased secretion. While it was found that the cases of hypopituitarism usually required a larger does for its production, this did not occur constantly, or in a sufficiently larger percentage to make it of value as a diagnostic sign.

The effect of posterior lobe secretions upon the other endocrine glands is not absolutely defined. The fact that a hypothyroid state is frequently associated with hypopituitarism, especially if it occurs in late adult life, which produces a combination that is believed necessary for the production of pituitary hibernation, has led to the conclusion that hypoactivity of the thyroid more frequently accompanies decreased function of this lobe. It has also been noted that peculiar hyperthyroid states have been frequently associated clinically with hyperpituitarism of the posterior lobe. This relationship may possibly be accountable for the increased basal metabolism and decreased sugar tolerance present in these cases, and it might help to explain the discrepancies which have existed in basal metabolism determinations made in pituitary disorders.

The adrenals are supposedly insufficient in the hypopituitary, and hyperactive in hyperpituitary disorders of this lobe. The peculiar pigmentation (chloasma) so frequently found about the hairline, angles of the mouth, eyes, lateral aspects of the neck and nipples, has been taken by the writer as a sign probably associated with the anterior lobe disorders, and not due to the adrenals. This is thought to be true on account of

TABLE III

CLASSIFICATION—DISORDERS OF THE PITUITARY GLAND

I. **Anterior Lobe**

A. **Hypo**activity

1. **Pre**adolescent
   a. A-neoplastic
   b. Neoplastic
   ..... **Lorain-Levi Type**

2. **Post**adolescent
   a. A-neoplastic
   b. Neoplastic
   ..... **Amenorrhea, Dysmenorrhea, Metrorrhagia** reacting to Anterior Lobe treatment. No signs of Posterior Lobe disorder

B. **Hyper**activity

1. **Pre**adolescent
   a. A-neoplastic
   b. Neoplastic
   ..... **Gigantism** (no signs of Posterior Lobe disorder)

2. **Post**adolescent
   a. A-neoplastic
   b. Neoplastic
   ..... **Acromegaly** (no signs of Posterior Lobe disorder)

II. **Posterior Lobe***

A. **Hypo**activity

1. Pars Intermedia (?)..... **Polyuria** (Bab) (Reaction to Pituitrin. Signs of Anterior Lobe and Pars Nervosa disorder absent)

2. Pars Nervosa..... Pituitary **Obesity** (Decreased metabolism, increased sugar tolerance. Polyuria and signs of Anterior Lobe disorder absent)

B. **Hyper**activity ..... Hypophyseal **Glycosuria** (Increased metabolism, decreased sugar tolerance. Polyuria and signs of Anterior Lobe disorder absent)

III. **Bilobar***

A. Anterior and Posterior Lobes

a. **Hypo**activity ..... **Froelich's Type** without, or with polyuria (Biedl)

b. **Hyper**activity ..... **Gigantism** or **Acromegaly** with **increased** metabolism and **decreased** sugar tolerance. Adiposity absent

c. **Hetero**activity

1. Anterior Lobe hyperactive
   Posterior Lobe hyperactive
   Gigantism or **Acromegaly** with **Polyuria**

2. Anterior Lobe hypoactive
   Posterior Lobe hyperactive
   Genital Aplasia, Nanism, Amenorrhea, etc., with **Pituitary Glycosuria** (Increased metabolism; decreased sugar tolerance)

*(1) Pre- and (2) Post-adolescent varieties and (a) A-neoplastic and (b) Neoplastic types are subdivisions under each activity (Hypo- and Hyper-) as given under I, Anterior Lobe.

its frequent presence in positive hypophyseal cases that are entirely free from other signs of adrenal disease, such as disturbed blood-pressure, marked asthenia, diarrhea, and other symptoms.

It has been stated by some authors (Fischer, Falta and others) that the hypersecretion of the posterior lobe has a marked inhibitory effect upon the gonads, as well as a stimulating effect upon the mammary gland. Personal observation in the writer's cases has led to the conclusion that Bell is probably correct in stating that this relationship does not exist. In those cases of pituitary disease in which the function of the gonads was disturbed, this was attributed to the hormone from the anterior, and not from the posterior lobe. Four cases with pure posterior lobe pituitarism, had marked changes in metabolism and carbohydrate tolerance, adiposity, etc., in which no abnormal changes, either in function or development, of the genitals could be demonstrated or were on record.

Pemberton and Sweet assign to the secretion of the posterior lobe an inhibitory influence upon the pancreatic secretion. It is known that there is a marked increase in the sugar tolerance in hypopituitarism, and yet there is an uncertainty of a hypoactivity of the pancreatic secretion in this condition. The nervous makeup of the individual is markedly affected in changes of activity of this lobe. In decreased secretion, apathy and somnolence are frequent. In hypersecretion, marked periodic psychic instability, of various degrees and moods, is very common. The temperature, pulse, and blood-pressure correspond well to the activity of any other endocrine gland, being subnormal in decreased secretion, and normal (or at times there is a slight pyrexia, hypertension, and tachycardia) in increased secretion of this lobe.

With the above physiologic effects serving as a basis for the "hormonic" signs of the secretory functions of these lobes, the accompanying classification has been evolved.

This classification, based solely upon the "hormonic" signs of hypophyseal disease, groups the disorders of this gland into three divisions, dependent upon whether one or both of the lobes were involved: (I) Anterior lobe disorders, in which this lobe alone was involved; (II) Posterior lobe disorders, in which this lobe, without clinical evidence of anterior

lobe dyscrasia, was affected; (III) Bilobar disorders, in which abnormal function of both lobes could be demonstrated. Each lobar division is subdivided into the activities prevailing, the anterior and posterior lobe disorders into the states of: (A) hypoactivity and (B) hyperactivity; the bilobar group into the states of: (A) hypoactivity, (B) hyperactivity and (C) heteroactivity. The last named (heteroactivity) comprises mixed cases, in which there were opposite secretory states of the individual lobes, such as hyperactivity of the anterior lobe, combined with hypoactivity of the posterior lobe, and vice versa. These activities are redivided into: (1) pre-adolescent and (2) post-adolescent varieties, dependent upon the age incidence of the abnormal secretory state. A final division is made of the age incidence, into: (a) a-neoplastic and (b) neoplastic varieties.

Under the pre-adolescent hypoactivity of the anterior lobe is grouped the Lorain-Levi type of pituitary insufficiency. This type has not yet received the distinction of a special group division. Others, besides Lorain and Levi (Meige, Allard, Rennie, Kumell, Falta, Bell), in fact, nearly all writers who have collected a series of cases, have described similar types, intimating that the types were due to simple and single insufficiency of the anterior lobe. These types are characterized by having a classical arrest of osseous growth, with complete aplasia of the genital system, without additional endocrine symptoms referable to the posterior lobe.

In the post-adolescent hypopituitarism of the anterior lobe, the writer has grouped those female cases which have had some osseous changes indicative of early anterior lobe disorder, and which developed, after the age of maturity, amenorrhea, metrorrhagia, or dysmenorrhea, dissociated from any local or general disease, that reacted completely to substitution treatment of anterior lobe extracts. Under the hyperactivities of this lobe are described the well-known clinical syndromes of gigantism and acromegaly. These differ from case illustrations ordinarily found in the literature, by having negative evidence of posterior lobe involvement, such as polyuria, adiposity, abnormalities of basal metabolism, carbohydrate tolerance and unstriped muscle contractions.

Under the posterior lobe dyscrasias, the differentiation between the opposite states of activity was not so clear-cut. There

is yet considerable uncertainty as to whether hypophyseal polyuria should be classified with the varieties of insufficiency or of overactivity of this lobe. These cases are most easily explained by Bab's theory, which attributes them to the pars intermedia insufficiency. The writer has observed 9 (of 11) cases of typical diabetes insipidus, reacting positively to hypophyseal extract treatment, 3 of which were free from other "hormonic" signs both of the anterior lobe and the pars nervosa disorders. This might be explained by defining a simple pars nervosa syndrome as consisting clinically, in the hypoactive state, of obesity, and in the hyperactive state, of increased basal metabolism and decreased sugar tolerance. On the contrary, it is true that the majority of the polyurias attributed to the hypophysis have other endocrine symptomatology connecting them with either the anterior lobe or the pars nervosa portion of the posterior lobe. The hypoactivity of the pars nervosa, independent of the pars intermedia, is given as pure pituitary obesity, not associated with "hormonic" signs of the anterior lobe or polyuria, but having positive evidence of a decreased basal metabolism and increased sugar tolerance. Under the hyperactive varieties of the posterior lobe is classed hypophyseal glycosuria. This is a glycosuria which can be differentiated from one due to pancreatic disorder or one associated with ductless gland dyscrasia. It has the usual increased metabolism and decreased sugar tolerance, but is free from polyuria and "hormonic" signs of anterior lobe disorder.

Under the bilobar divisions are grouped those cases in which there is a concomitant anterior and posterior lobe disorder existing in the same individual. In order to include all cases thus represented, three activities must be considered: (1) hypoactivity of both lobes; (2) hyperactivity of both lobes and (3) heteroactivity, in which the lobes have an opposite secretory function. Under hypoactivity, Froelich's disease, either with or without polyuria (the former as described by Biedl) is classed. Under hyperactivity, those cases of gigantism or acromegaly and glycosuria, with which are associated increased metabolism and decreased sugar tolerance, without adiposity, are grouped. This classification takes many of the cases of both gigantism and acromegaly out of the simple anterior lobe dyscrasia variety, for it has been well known for many years that a large percentage of

these cases have been associated with posterior lobe symptoms, such as polyuria, glycosuria, and disturbance of metabolism and sugar tolerance. Nevertheless, they have been classed by many authors either as simple anterior lobe dyscrasias, or have been grouped under the gross term "pituitary dystrophy."

The heteroactive varieties of bilobar pituitarisms should contain those cases in which the individual lobes of the hypophysis have opposite activities. For instance, gigantism or acromegaly, associated with polyuria, a not infrequent variety, should naturally be placed in this bilobar variety. Another considerable percentage of these diseases shows evidence of anterior lobe hyposecretion (such as genital aplasia and infantilism, amenorrhea, sexual impotence, muscle fatigue, and mental apathy), associated with posterior lobe hyperactivity (such as pituitary glycosuria, with increased metabolism and decreased sugar tolerance). It is the hope of the writer that this conception of a heteroactive bilobar division will be the means of disentangling many of the so-called dyspituitarisms and dystrophies, which have been so ill-defined that they add only confusion to the efforts toward diagnosis and treatment.

BIBLIOGRAPHY

Anton: Vier Vorträge über Entwicklungsstörung beim Kind. Berlin, 1908. Reiner Psychoinfantilismus; Forens. Psychiatrie, 1910, 2.

Aub, J. C. and Du Bois, E. F.: Clinical calorimetry, nineteenth paper. The basal metabolism of old men. Arch. Int. Med. (Chgo.), 1917. **19,** 823-831.

Bab, H.: Die Hypophyse als Regulator der Diurese und des spezifischen Gewichts des Harnes. Münch. med. Wchnschr., 1916, **63,** 1685, 1721, 1758.

Bauer, A.: Infantilisme et chétivisme. Presse méd. (Paris), Dec. 4, 1909, 870-872.

Bell, W. Blair: The Pituitary, 1919, Part I, p. 79, Incidence, The physiology of the pituitary; Ibid., p. 237; Incidence, Hypopituicarism occurring before puberty; Ibid., pp. 158-177; Incidence, Effect of posterior lobe secretion upon the gonads.

Biedl, A.: Innere Sekretion. Urban u. Schwarzenberg, Wien u. Berlin, 1913, 534 p., 8 pl.; 694 p., 6 pl. 8°.

Bramwell, B.: Infantilism: no apparent cause. Clin. Stud., 1908, **6,** 389-392.

Brissaud, E.: L'infantilisme vrai; Icon. de la Salpêtrière (Paris), 1907, **20,** 1-17.

Brissaud, E. and Meige, H.: Gigantisme et acromégalie. Rev. scient., 1895, **3,** 330-336. Ibid., Type infantilé du gigantisme. N. icon. de la Salpêtrièrie (Paris), 1904, **17,** 165-172; Rev. neurol., 1904, **12,** 191-194.

Crowe, S. J., Cushing H. and Homans, J.: Experimental hypophysectomy. Bull. Johns Hopkins Hosp. (Balt.), 1910, **21,** 127-169; Effects of hypophyseal transplantation following total hypophy-

sectomy in the canine. Quart. J. Exper. Physiol. (Lond.), 1909, **2,** 389-400.

Cushing, H.: The functions of the pituitary body. Am. J. Med. Sc. (Phila.), 1910, **139,** 473-484.

Dyspituitarism. Harvey Lecture (N. Y.), 1911, pp. 31-46.

Diabetes insipidus and the polyurias of hypophyseal origin. Shattuck Lecture. Communications, Med. Soc., Boston, 1913, **24,** (Part 1), 23-49.

Address on Surgery: Realinements in greater medicine, Their Med. J. (Lond.), 1913, (ii), 290-297.

Partial hypophysectomy for acromegaly; with remarks on the function of the hypophysis. Ann. Surg. (Phila.), 1909, **1,** 1002-1017.

Cushing, H. and Goetsch, E.: Concerning the secretion of the infundibular lobe of the pituitary body and its presence in the cerebrospinal fluid. Am. J. Physiol. (Balt.), 1910, **27,** 60-86.

Hibernation and the pituitary body. Abstr. Proc. Soc. Exper. Biol. and Med. (N. Y.), 1913-14, 11, 25.

The pars anterior and its relation to the reproductive glands. Abstr., Ibid., p. 26.

Hibernation and the pituitary body. J. Exper. Med. (N. Y.), 1915, **22,** 25-47, 2 pl.

Du Bois, D. and E. F.: Clinical calorimetry; tenth paper. A formula to estimate the approximate surface area if height and weight be known. Arch. Int. Med. (Chgo.), 1916, **17,** 863-871.

Falta, W.: The ductless glandular diseases. Falta and Meyers, pp. 229-328.

Fischer, B.: The ductless glandular diseases. Falta and Meyers, p. 317.

Janney and Isaacson: Blood sugar tolerance test. J. Am. M. Ass. (Chgo.), 1918, **70,** 1131.

Kumell, R.: Zur Kenntniss der Geschwülste der Hypophysengegend. München. med. Wchnschr., 1911, **58,** 1293-1298.

Levi, E.: Contribution à l'étude de l'infantilisme du type Lorain, N. icon. de la Salpêtrière (Paris), 1908, **21,** 297, 421.

Meige, H.: L'infantilisme. Gaz. d. hôp. de Paris, 1902, **22,** 207.

Pemberton, R. and Sweet, J. E.: Further studies on the influence of the ductless glands on the pancreas. Arch. Int. Med. (Chgo.), 1910, **5,** 466-481.

Rennie: Endothelioma of the pituitary gland with infantilism. Brit. Med. J. (Lond.), 1912, (i) 150.

Rohdenburg, G. L., Bernhard, A. and Krehbiel, Otto: A study of sugar mobilization based upon 228 human cases. Am. J. Med. Sc. (Phila.), 1920, **159,** 577-586.

HEMORRHAGIC SYNDROME CURED BY THYROIDIN*

Louis P. Bottaro,
Director of the Gynecological Clinic in Maciel Hospital
and
J. C. Mussio Fournier,
Chief of the Medical Clinic of the Faculty of Medicine, Montevideo

Although much has been written upon the subject of thyroid opotherapy, the indications for this treatment are still so indeterminate as to demand many more data. The following is a report of a case in which severe hemorrhagic manifestations were successfully controlled by the use of thyroidin.

The patient is a woman twenty years old, under-weight and whose hereditary antecedents are of no importance. Menstruation commenced at eleven years, was profuse and usually lasted twelve days, during which time severe epistaxis occasionally occurred. Using thyroidin the menstruation period was reduced to three days and the nasal hemorrhages arrested. As soon as the patient ceased taking this product the disturbances returned.

When she was about 12 years old her eyebrows began to fall out. At 14 years of age she gave birth to a child, and during childbirth acquired a puerperal infection, causing cervicitis and adnexitis. From this time until she was 19 years old the patient suffered three induced abortions and a mercurial intoxication, the latter producing a mild nephritis of which she was cured.

During the periods when opotherapy was omitted the patient suffered from otorrhagia and sub-conjunctival hemorrhage in addition to the other hemorrhagic disturbances. Owing to her negligence an acute hemorrhagic attack occurred, signalized by metrorrhagia, epistaxis, hemoptysis and purpura; this was resistant to the classic coagulative treatment. One of us then thought of using thyroid opotherapy, which was successful in arresting the hemorrhages. This once accomplished, clinical examination proved the existence of the adnexitis already mentioned.

---

*This paper has appeared elsewhere. It was accepted before the rule of exclusive publication was announced.

Laboratory tests disclosed the following conditions.

Urine, normal.

Wassermann reaction in the blood, negative.

Thorax, by radioscopy, normal.

Hemoglobin	85%
Coagulation and retraction of blood coagulum	Normal
Red corpuscles	4,170,000
White blood corpuscles	8,600
Neutrophiles	62%
Eosinophiles	6%
Basophiles	1%
Lymphocytes	25%
Large mononuclears	5%

DISCUSSION

Our patient had a pale, swollen face and an abnormal tendency toward vasodilatation phenomena in her cheeks. The falling of the eyebrows combined with the above was the only symptom of the minor hypothyroidal syndrome so well described by Levi and Rothschild (1).

We believe the case is probably a form of dysthyroidism, a diagnosis which, although it cannot be assured, should be considered, more especially in view of the remarkable results obtained with the thyroid therapy.

In a previous publication (2) we have insisted upon the desirability of taking much notice of those minor symptoms, so that we may finally be able to make a positive diagnosis when the aborted forms of hypothyroidism are encountered.

Without further discussion we wish merely to mention that Hertoghe (3) Werklen and Walther (4), and Max Perlsée (5) demonstrated some time ago the existence of hemorrhagic conditions in hypothyroid cases. These may result from dyscrasic alterations, or as one of us (6) has demonstrated contemporaneously with Levi (7), from congestive phenomena. Moreover, it is apparent that in some cases of hemorrhage that cannot as yet be attributed exclusively to a thyroid origin the success of thyroid therapy has been no less remarkable. This is evidenced by Sheffler's (8) observations on Werlhof's purpura, and by the studies of Taylor (9) and Marcel Labbé (10) in hemophilia.

In conclusion, although we are unable definitely to assert that the origin of this hemorrhagic complex lies in a purely thyroid dysfunctioning, it is nevertheless certain that the results secured emphasize the practical importance of thyroid therapy, whatever its form of action.

BIBLIOGRAPHY

1. Leopold-Levi and Rothschild H. de: La petite insuffisance thyroidienne. Paris, 1913, 309 p.
2. Mussio Fournier, J. C.: Cecité par double nevrité optique chez une malade atteinte d'hypothyroidisme; amelioration remarquable obtenue par la glandothyroine. Ann. d'ocul. (Paris), 1918, **155,** 265-271; Semana med. (Buenos Aires), 1919, **26,** 139-145.
3. Cited by Maurice Perrin, Les Sécretions Internes, leur influence sur le sang, p. 72.
4. Merklen, P. and Walther, Ch.: Sur un case de myxoedeme amélioré par la greffe thyroïdienne. Bull. mem. soc. med. Hôp. (Paris), 1890, **7,** 859-864.
5. Perlsée, M.: Opotherapie thyroïdienne contre les menorrhagies et en particulier les hemorrhagies de la menopause. Semaine médicale (Paris), 1907, **27,** 298.
6. Mussio Fournier, J. C.: Forma congestiva del hipotriodismo. La Prensa Med. Argentina (Buenos Aires), 1918, **4,** 463.
7. Levi, L.: Neuro-arthritismè a fluxions multiples par instabilité thyroïdienne. Presse méd. (Paris), 1918, **26,** 191-193.
8. Scheffler: cited by Perrin, (3).
9. Taylor, W. J.: The internal use of thyroid extract to increase coagulation of the blood. Monthly Clyclopedia (Phila.), 1905, **8,** 298-300.
10. Labbé, M.: L'hemophylie. Congres de Méd. (Paris), 1901, p. 130.

PUBERTAS PRECOX WITH ESPECIAL ATTENTION TO MENTALITY*

Joshua H. Leiner

Adjunct Attending Neurologist, Lebanon Hospital and Central Neurological Hospital, Blackwell's Island, New York.

Pubertas precox is a syndrome manifested by premature maturity, anatomically, physiologically, and often mentally, as a result of faulty metabolism induced, supposedly, by endocrine disturbances.

That this condition was recognized by the ancients is beyond doubt. For the first account of the condition recognizable as a clinical entity we must go back to Craterus, the brother of King Antigonus (1), who writes: "The subject was an infant, a young man, a mature man, an old man, was married and begat children and all in the space of seven years."

Pliny the elder, who lived in the reign of Vespasian, handed down the history of certain remarkable children; he states: "It is well known that there be some that naturally are never but a foot and a half high, others again somewhat longer, and to this height they came in three years, which is the full course of their age, and then die. We read, moreover, in the chronicles, that Salams, one Euthimenes, had a son who, in three years, grew to be three cubits or four and a half feet high, but he was in his gait slow and heavy, and in his wit as dull and blockish, howbeit in the time overgrown he was, and his voice changed to be great, and at three years he died suddenly of a general cramp" (2).

In 1747 Mead (3) presented before the Royal Society of London, a patient who was "remarkable for his bulk and height," and also for the external marks of puberty, which were first observed at the age of twelve months. At the age of five he had pthisis pulmonalis and died in a few months. "He had when dead the appearance of a venerable old man."

One of the first well observed cases was recorded over a century ago by Anthony White (4). He presented "Philip Howarth in whom signs of puberty commenced at an early age."

*Read before the New York Neurological Society April 6, 1920.

The family history was negative, gestation was normal, and he was the ninth child born. At birth he had a full crop of hair; the sutures of his cranium were closed, but a slight fontenalle was palpable. At the end of the first year a change took place; his hair had grown to a great length, he grew pale and ugly in appearance. Small hairs appeared on his pubis; his testes and penis increased in size, and his voice altered. White, who was keenly interested in the lad, invited him to his home for further observation. He states: "On first view of the boy the manly character, strongly expressed, is extremely striking. His voice is like that of a young man of sixteen years and he can whistle very low tones; his laugh is loud. There was no hair on his chin, but steatomatous matter was present which usually makes its appearance preceding the growth of a beard. His teeth were spaced (how many not recorded); the nipples were prominent; no hair was visible in the axilla, but there was an odor emanating as that of an adult. His height was three feet, two inches and he weighed 47 pounds, i. e., at two years. At three years his height was three feet, four and a half inches and his weight was three stone, nine and a quarter pounds, or fifty-one and a quarter pounds." He was observed to have an understanding of a six-year-old child and, quoting this keen observer, "many of his observations and inquiries appeared to have been the result of mature reflection. It must, however, be observed that his general character was marked with a considerable mixture of childish playfulness. He was mild and not easily provoked to anger. When, however, his rage was excited, it was not expressed in the usual manner of children, but by the lowering of the eyebrows, the shaking of his head and with uplifted fist. He had a talent for music and sang with correctness."

The factor of hereditary transmission is apparent in the following two cases. Plumb (5) delivered a mature looking child whose facial appearance was feminine, and gave the impression of a delicate twelve-year-old child. Her external genitalia were developed as those of a child of seven to eight years, and her form was that of a fifteen-year-old girl. Her head was covered with thick, beautiful, brown curly hair which was three to four inches in length. There was no hair in the axilla. What was more remarkable was the beginning of menstruation when she was six weeks old. She menstruated for two and a half days

each month thereafter. At the time the case was recorded, she was ten months old and perfectly well. The child's clitoris was so long as to necessitate amputation. The parents of this child were both very vigorous sexually. Irion (6) reported a similar case in which menstruation first appeared seven days after birth; the patient showed the characteristic nervous phenomena when she skipped a period.

In the following case reported by Stone (7), there is a direct history of pubertas precox in the father. The subject when dressed gave the impression of a ten-year-old lad; he was actually four years old. When he disrobed, he looked the typical Infant Hercules, showing a fine physical development of a young man of 21. He was 4 feet, ¼ inch tall and weighed 70 pounds. His secondary sexual characteristics were fully developed. Mentally, the boy showed a lively intelligence; he was very talkative at home, but shy with strangers. His speech seemed to be imperfect. He was nearly always in good humor, but when angry settled his quarrels with old-fashioned "knock-down blows." The father, as mentioned above, was prematurely developed, and his first sexual indulgence occurred at the age of eight. He stated that between the age of ten and thirteen, "he was a better man than he has ever been since." Rogers also quoted a number of cases that showed the factor of heredity.

The direct causative factor of precocious puberty is hypersecretion of either the gonads, pineal gland or adrenal cortex, as indicated by hyperplasia or neoplastic development. That the pituitary and thyroid are also concerned, secondarily, however, is unquestionable. It will be necessary, therefore, to divide the cases of premature precocity into those that have acquired this syndrome through neoplasms and those due to hyperplastic states.

Ovarian Type. Rogers has collected 101 cases of pubertas precox; of these 81 subjects were females and 20 males. Of the 81 female cases, 73 appear to be due mostly to hyperovarianism. The cases of Krabbe (8), Wells (9), Lenz (10) and Bruno Wolff (11), were also of this type. Lenz's case was studied very carefully. He first saw the child when she was six and one-quarter years old. Menstruation had begun at 16 weeks. The secondary sex characteristics were those of a mature woman. She was shy and easily embarrassed. She went to school and was a good pupil.

She played with children of her own age and was childish in activity. She was again seen when twelve years old, when she appeared to be twenty-two. Her behavior was still childish, and extraordinarily shy. She was still playing with dolls. She cried pitifully when the other children teased her about her large breasts.

An instance of neoplasms of the ovary producing pubertas precox is recorded by Lucas (12). The little patient was seven years old and showed all the signs of genito-somatic maturity and early menses. A tumor of the ovary was diagnosed and after its removal all the signs of adolescence and menstruation disappeared. Blair Bell (13) quotes Roger Williams, who collected eleven cases of sexual precocity in female children, due to neoplasms of the ovary. However, one should not draw the conclusion from this that all ovarian tumors in young children necessarily lead to sexual precocity. There must be other factors entering into this mechanism.

To summarize the mental traits and habits in these ovarian cases, it can be said that none show mental precocity. In fact, the subjects are of a low mental type. They speak, play and act in accordance with their true age. The girl reported by Lenz (10) still played with her dolls, although she gave the physical impression of a girl of twenty-two. They learn well at school, but they show no "old-fashioned" way of thinking, as Krabbe (8) puts it. Neurath (14), who had a considerable opportunity to observe them, also comes to the conclusion that their psychic condition is not so far advanced as their physical. That some of these children put away their toys and become seclusive is to be ascribed to self-consciousness rather than to any mental maturity

Adrenal Cortex Types. The clinical picture differs here, according to whether the male or female is involved. When there occurs hyperplasia of the adrenals in the male, it tends to accentuated masculine precocity. When it occurs in the female it tends to change the female into the male type, and to give her the secondary sexual characteristics of the male.

In a case reported by Marchand (15), a girl was baptized as a male. As a result of a medico-legal examination, it was found that her body showed a spurious hermaphrodism with hair over face and body, and a clitoris as large as a penis. At autopsy

she showed hypertrophy of the adrenals, and particularly of the cortex.

Tumors of the Adrenal Cortex. Pitman (16) reported a girl of three who showed nothing child-like in either voice or manner. She often seemed idiotic, but aggressive. She showed bushy eyebrows and a moustache in addition to other male characteristics. A tumor of the adrenal cortex was found.

Bulloch and Sequeira (15) collected 12 cases of adrenal tumors. Ten were found in the female and two in the male. Orth (15) reported the case of a girl of 4½ years, who had so much hair on her face that she had to be shaved. The clitoris was the size of a small penis. She had a neoplasm of the right adrenal. In Dobbertson's (15) case, a girl had a mass of hair on her back. Glynn (17) reports the case of a girl of 7. She had the appearance of a young man, with a black silky beard, a moustache and whiskers.

These cases therefore show uniformly hypertrichosis of the male type. All manifest a large clitoris, which shows the tendency towards male sexuality, and all showed an absence of menstruation, with the exception of one case reported by Bulloch and Sequeira (15), in which menstruation appeared at the age of a little more than ten years. The appearance of menstruation at this time can hardly be classed, however, as precocious.

A case of adrenal origin in a boy of 5½ is reported by Linser (15). The physical development was that of from 16 to 18. Sex characteristics were of the male type. The pineal, pituitary and thyroid glands were found to be normal.

As regards mentality and habits in these cases, the literature is far from satisfactory. It indicates, however, that while they show some aggressiveness, in the main, their psychic condition is below par. Pitman states that his case showed idiocy; Bulloch and Sequeira and Colcott Fox (15) state that their cases showed a dullness of intellect. Glynn's patient was dull and apathetic; she took no interest in her surroundings and would answer questions only if they were frequently repeated.

Hypergonadal Condition in the Male. Sarchi (18) published a case that showed a malignant tumor of the left testicle. At 5, the testicle was as large as that of an adult. The boy grew rapidly, his voice grew to a deep bass, and hairs appeared on his genitals. At 9 years, he was 143 cm. in height and weighed 44

kilograms. The left testicle was removed and an alveolar carcinoma was shown. Four months after the removal, his beard disappeared, his voice again became child-like and his genitals were getting smaller. His sexual impulses, emissions and erections ceased. His character in general reverted to the childhood stage.

A case of hypergenitalism was reported by Strauch (19) of the Cook County Hospital. In this instance no anatomico-pathologic changes were found. No cerebral symptoms were present. No tumor of the pineal was suspected. The boy was 11½ years old and had previously shown mental retardation. His genitals, including the prostate and seminal vesicles, were developed as in an adult, but no spermatozoa were found. His voice was strikingly deep. As to his psychic condition and habits: He was irritable and nervous, and cried whenever his mouth had to be examined. He was stubborn, disobedient, troublesome and showed a resentful disposition towards other children. At home he played with boys younger than himself. There was no evidence of sexual shame, nor was there any visible propensity for the other sex. He could not count to more than five, and even then he had to be helped. His handwriting was not legible, nor could he write his own name without having a copy placed in front of him. He attended school for three years, and he could not execute a simple example of addition, nor did he remember his songs or prayers.

Morse (20) reports a boy of 23 months with genito-somatic precocity and delayed mentality. An X-ray examination of the skeletal system revealed the bony development of a 6½-year-old boy. No spermatozoa were found in the emissions. Woods (21) and Lopez (22) report cases that are of undoubted hypergonadal origin. Both subjects showed remarkable strength. The former was 6¾ years old and was nearly 5 feet tall. He was so mischievous and full of animal spirits that he had to be placed in an industrial school. It took three policemen to get him there. The latter subject was a colored boy of 3 years and ten months; he showed genito-somatic precocity and lifted a man of 140 pounds from the ground with ease. The case of Gilbert Brechet (23) should also be included here.

The mentality and habits in these cases show no precocity. In fact, the subjects are retarded and, according to Moreau (24), Hofacker (25), Hudoverning and Popovitz (26), Ziehn (27) and Neurath (14), may even show idiocy and imbecility. Neurath, who reported 27 cases of this type, is quoted by Strauch (19), that "in most cases there existed the psychic function of their infantile age."

Pineal Tumors. Neoplasms of the pineal gland have drawn attention to the subject of pubertas precox, as no other condition has. The opinion once prevailed that pineal tumors exist only in the male. This, however, has since been disproven. Baily and Jellife (28) collected and reported in an excellent paper 59 cases of pineal tumors, together with an additional case of their own, making 60 in all. Seventeen cases showed involvement up to the age of 16. Fourteen of these occurred in the male and three in the female.

There is this to be said in reference to tumors producing precocious puberty, that while the pineal tumors occur predominantly in the male, tumors of the adrenals as hypernephromata, occur five times oftener in the female.

I must agree with Gordon (29) that the histories of the recorded cases are inadequate, not only as regards pineal tumors, but all the subject matter herein discussed. The clinical observations are too meagre, often, for correct endocrine interpretation, and it seems the further back one goes the more illuminating and keener are the clinical observations of the writers.

The following cases of pineal tumors bear on our subject.

Aesterich and Slawyks (30) report a boy who was a still birth baby, as a result of forceps delivery, but who developed normally during the first year of life. Convulsive attacks then set in. At 3, this child, who was formerly bright, became strikingly quiet and shy and sat in the corner and cried. Genitosomatic precocity then became apparent. Mentally he was somewhat precocious,—what the Germans call "altklug." This boy displayed no onanism.

Von Frankl-Hochwart (31) reported a boy who, at three, grew with excessive rapidity and showed mental precocity. At 7 years, his precocity was astonishing. He pondered and discussed at length the immortality of the soul and the life after death. This case made such an impression on Dana and Berkely (32), that it led to the well-known feeding experiments on the mentally backward children in the New York Public Schools and to the experimental work at Vineland by Goddard (33). At autopsy, in the case mentioned, a teratoma of the pineal was found. In fact most of the tumors of the pineal are teratomas.

Baily and Jellife (28), who went into the mental study of their case much more than any of the other writers, state that the boy who was formerly bright in school work began to show a failing memory. He also grew more reserved and apathetic. He showed a tendency towards depression and cried often. The Zeihn test "revealed a lack of retention, with a marked slowing of all responses."

Gauderer (28) reports a boy of 12 who had a fixed expression, was apathetic and who answered questions slowly but clearly.

Raymond and Claude (30) report the case of a boy of 10, who was mentally apathetic and answered questions well, even slightly better than most boys of his age. His memory was good, but he showed a slight depression.

Kidd (30) reports the following cases, by Pellizzi and Machell. The first case of Pellizzi showed genito-somatic, together with mental precocity; the other case did not. The first subject, although only 2 years old, had seminal emissions that contained spermatozoa. Onanism was not present.

Machell reports two cases, one of which was interesting. This boy at 17 months had erections and emissions. In addition to his genito-somatic precocity, he showed marked mental precocity. At 44 months of age, he showed a disdain for the toys of small children. His habits bespoke an older boy. His manner was independent; he was perfectly self-possessed with strangers, and his answers to questions were given in a loud, bass, stentorian voice.

Kidd (30), although he wrote a thorough review of the literature, historical, clinical, experimental, etc., of the pineal, mentioned nothing concerning the mentality in pineal involvement.

From a comprehensive study of the literature, by which the various types of puberatas precox were classified, together with their respective mentalities, it can be said that mental precocity is non-existent, aside from its manifestation in the pineal type. In fact, there is in the major number a hypo-mental state, which gradually shades off into absolute idiocy. The subjects are in the main childish, and their mentality bespeaks their true age. In those cases, in which, through tumor growth, intracranial pressure is produced, various degrees of mental disorder arise, but such are scarcely germane to our discussion.

A trait common to all cases of precocity is the reserve, thoughtfulness, or quiet they manifest. They like to sit in a corner by themselves. Stanley Hall (34), in speaking of the psychic traits attending normal puberty, states that, "Inner absorption and reverie is one marked characteristic of this age and transition." This observation can, I believe, be applied to our cases, and is not in itself indicative of abnormality. Some writers believe that early sexual desire is a sign of mental precocity. This I believe is incorrect. It is purely an instinct.

DIAGNOSIS

To reach a diagnosis as to the particular gland involved primarily, and especially if there is any tendency towards readjust-

ment, one must: (1) have the cases under close clinical observation; (2) study their metabolism, particularly, as Blair Bell has advised, the calcium output, and (3) make Roentgen ray examinations for skeletal development and for the disappearance of the epiphyseal lines, as shown by Krabbe (8), Lenz (10) and Timme (35).

The approach to a correct diagnosis is somewhat difficult at present, in view of the fact that glandular structures that are seemingly antagonistic, produce nevertheless the common syndrome, precocious puberty. However, upon analysis there are always found some points of difference in respect to the particular gland involved.

Gonadal Type. In the female type due to hyper-ovarianism we always get early menstruation. This leads to excess calcium elimination, and therefore we find the subjects (if of pure ovarian type) always short in stature. If the skeletal system is examined by Roentgen ray, we find the epiphyses of the long bones closed. This fact is borne out clinically, that girls who menstruate early are usually short and those who menstruate late are tall. This tends to hold for races as well as individuals. Again the distribution of the hair is of the female type, as are the secondary sex characteristics, facies and form.

In the masculine gonadal type there is also short stature, concomitant with closed epiphyses, marked male secondary characteristics, deep voice, enlarged prostate and seminal vesicles and often emissions, either sterile or containing spermatozoa. What seems characteristic of this type is the marked physical strength manifested.

Adrenal Type. In the female we find marked hypertrichosis and secondary characteristics of the male type,—large clitoris, male facies and absence of menstruation. The case of Irion is an exception.

While we were always taught that the cortex of the adrenal has for its function the production of sex characteristics only, the work of Cramer (36) indicates that the cortex also participates in the production of adrenalin. The question of blood pressure should therefore be taken into account in a differential diagnosis.

The male adrenal type is difficult to differentiate from the gonadal except, perhaps, by their stature. Both types manifest accentuated male characteristics.

Pineal Types. In these the Roentgen plates should portray a shadow due to the acervalus cerebri, as a result of early involution, as shown by Boas, Scholtz (37) and Timme (38). Whether pure hyperplasia of this gland should give precocious puberty, as indicated by the work of McCord (39), Dana and Berkeley

(32), etc., or hypoplasia or recession of the gland according to Marburg, it is at present impossible to say.

Finally one may say that there are undoubtedly individuals living today, who were cases of pubertas precox, and undetected as such, who will undoubtedly live to a ripe old age. What takes place here is a compensatory readjustment of the excessive secretions by their antagonists, just as we see in the ultimate adjustment in the syndrome of thymus, pituitary and adrenal of Timme (35).

CONCLUSIONS

The literature as a whole supports the following conclusions.

1. Pubertas precox arises in certain individuals, whose progenitors show a particular type of endocrine imbalance.
2. The condition may arise in utero, or as a result of functionating rests, i. e., tumors, later in childhood, previous to puberty.
3. The entire internal glandular system is involved, but primarily the gonads, pineal and adrenal cortex.
4. Gonadal types predominate, then follow the pineal, and last, the cortico-adrenal.
5. Pineal types occur mostly in the male; cortico-adrenal and gonadal in the female.
6. Mental precocity is very rare and is found only in those in whom the pineal is primarily involved, and then only in the male.
7. The mentality in the other types is either unaffected or retarded.
8. The manifest mental precocity is of the child-like, imaginative form, and has no real substantial basis.
9. With early diagnosis in the hyperplastic type, readjustment can be aided materially by proper endocrine therapy.

BIBLIOGRAPHY

1. Greek translation, Phlegon de Mirabilia, Cap. xxxii; Cf. White (4), p. 277.
2. Pliny, Philemon Holland, translator, Book ii, Chapt. xvi. Cited by White (4).
3. Quoted from Anthony White (4).
4. White, Anthony: Historical account of Philip Howarth, a boy in whom signs of puberty commenced at an early age. Med. Chir. Trans. (London), 1809-11, **1-2,** 276-285.
5. Plumb, P. E.: Precocious menstruation; a unique case. N. Y. Med. J., 1897, **65,** 768.
6. Irion, J. W.: A case of precocious menstruation. Ibid., 1896, **64,** 227.

7. Stone, R. K.: Extraordinary precocity in the development of the male sexual organs and muscular system in a child of four years. Am. J. Med. Sc. (Phila), 1852, **24,** 561-564.
8. Krabbe, K. H.: Early synostosis of the epiphyses with dwarfism in pubertas precox. This Journal, 1919, **3,** 459-466.
9. Wells, G.: A remarkable case of early and continued menstruation. Maryland M. J. (Balt.), 1902, **45,** 440.
10. Lenz, J.: Vorzeitige Menstruation Geschlechtsreife und Entwickelung. Arch. f. Gynaek. (Berlin), 1913, **99,** 67-144.
11. Wolff, Bruno: Zur Kenntnis der Entwicklungsanomalien bei Infantilismus und bei vorzeitiger Geschlechtsreife. Arch. f. Gynaek. (Berlin), 1911, **94,** 542-579.
12. Lucas, R. C.: A case of tumor of the right ovary in a child of seven, associated with precocious puberty. Med. Press & Circ. (London), 1888, n. s. **45,** 459. Trans. Clin. Soc., Lond. 1888, **21,** 224.
13. Bell, W. Blair: The sex complex, Wm. Wood & Co., N. Y., 1916, p. 149.
14. Neurath, H.: Die vorzeitige Geschlechtsentwickelung, Ergebn. f. inner. Med. u. Kinderheilk., 1909, **4,** 41-81.
15. Bulloch, W. and Sequeira, J. H.: On the relation of the suprarenal capsules to the sexual organs. Trans. Path. Soc. Lond., 1905, **56,** 189-208.
16. Pitman, H. A.: General melasma and short hair over the entire body of a child of three years, with conversion of the left suprarenal capsule into a large malignant tumor; the external organs of generation resembling those of adult life. Lancet (Lond.), 1865, (i), 175.
17. Glynn, E. E.: The adrenal cortex; its rests and tumors, its relation to other ductless glands and especially to sex. Quart. J. Med. (Oxford), 1911-1912, **5,** 157-192, 1 pl.
18. Sacchi, E.: Di un caso di gigantismo infantile (pedomacrosomia) con tumore del testiculo. Arch. di ortop. (Milano), 1895, **12,** 305-318.
19. Strauch, A.: Sexual precocity in the male. Am. J. Dis. Child. (Chicago), 1918, **15,** 132.
20. Morse, J. L.: Case of abnormal physical and sexual development in an infant of two years, probably due to a tumor of the pineal gland. Arch. Pediat. (N. Y.), 1913, **30,** 179.
21. Woods, T.: An extraordinary case of early puberty in a boy. Lancet (Lond.), 1882, (ii), 337, 473.
22. Lopez, A.: Case of remarkable precocity in a male. Am. J. Med. Sc. (Phila.), 1843, **5,** 500.
23. Breschet, Gilbert: Description d' un enfant de trois ans offrant tous les signes de la puberté. Bull. Fac de Méd. de Paris, 1820-21, **7,** 98-111.
24. Moreau, J. L.: Fragment d' une notice sur un jeune homme de onze ans, chez lequel on observe tous les signes extérieurs de la virilité, accompagnés de l' accroissement extraordinaire d' un état pathologique du testicule. J. de Med. Chir. et Pharmacal. (Paris), 1806, **12,** 274-278.
25. Hofacker, C.: Ein seltener Fall von Frühreife mit Menstruatio praecox. Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte, 1898, (Leipz.), 1899, **70,** Pt. 2, 2. Hefte., 182.
26. Hudoverning, C. and Popovits, U. P.: Gigantisme précoce avec développement précoce des organs génitaux. N. inconog. de la Salpêtrière (Paris), 1903, **16,** 181-192.

27. Ziehn: Fall von Gigantismus. Berlin. klin. Wchnschr., 1906, **43,** 1198-1199
28. Baily, P. and Jellife, S. E.: Tumors of the pineal body; with an account of the pineal syndrome, the report of a case of teratoma of the pineal and abstracts of all previously recorded cases of pineal tumors. Arch. Int. Med. (Chgo.), 1911, **8,** 851-880.
29. Gordon, M. B.: The role of the pineal in pediatrics. This Journal, 1919, **3,** 437-453.
30. Kidd, Leonard J.: The pineal body; a review. Med. Chronicle, (Manchester), 1912, **57,** 154-184.
31. von Fränkl-Hochwart, L.: Uber Diagnose der Zirbeldrüsentumoren. Wiener med. Wchnschr., 1910, **60,** 505-508.
32. Dana, C. L. and Berkely, W. N.: Functions of the pineal gland. Med. Rec. (N. Y.), 1913, **83,** 835.
33. Goddard, H. H.: The Vineland experiment with pineal gland extract. J. Am. M. Assn., (Chgo.), 1917, **68,** 1340.
34. Hall, G. Stanley: Adolescence; its psychology, etc., N. Y., 1904.
35. Timme, Walter: A new pluriglandular compensatory syndrome. This Journal, 1918, **2,** 209-240.
36. Cramer, W.: A histochemical method for the demonstration of adrenalin granules in the suprarenal glands. J. Physiol., (Lond.), 1918, **52,** viii-x; Abst., This Journal, 1919, **3,** 496.
37. Boas, E. P. and Scholtz, T.: Calcification in the pineal gland. Arch. Int. Med., (Chgo.), 1918, **21,** 66.
38. Timme, Walter: Progressive muscular dystrophy as an endocrine disease. Ibid., 1917, **19,** 79.
39. McCord, C. P.: The pineal gland. Trans. Am. Gyn. Soc., 1917; Surg. Gyn. and Obstet., (Chgo.), 1917, **25,** 250.
40. Horrax, Gilbert: Studies on the pineal gland; Arch. Int. Med., (Chgo.), 1916, **17,** 607, 637.

THE ENDOCRINE SECRETION OF HEN-FEATHERED FOWLS

T. H. Morgan

Professor of Experimental Zoology, Columbia University, New York

In the older literature there are many references to changes that have been noticed in old hens and female pheasants that make these birds more like the males of their species. They become quarrelsome, they sometimes crow, the feathers change their color, etc. It has been recorded in several cases that these changes appear after the female has ceased to lay, and in a num-

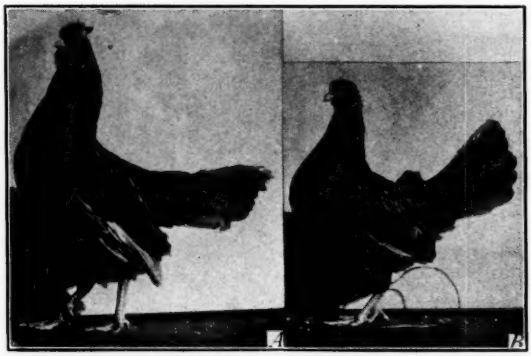


Fig. 1, A. Sebright Bantam male; B. Sebright Bantam female.

ber of cases that the change was associated with a diseased condition of the ovary. Complete removal of the ovary of birds is a difficult operation owing to its irregular shape and to its close adherence to the body wall. Goodale has succeeded, nevertheless, in completely removing the ovary of young fowls. When the adult plumage develops in such birds it is like that of the cock of their breed. In the Leghorns, where the difference between the sexes is very great, the result is most striking. The comb and wattles, and the spurs also, grow larger than in the normal hen. Evidently something produced by the ovary—some internal secretion perhaps—inhibits the full development of the

plumage of the hen, of her comb, and sometimes also of her spurs.

Castration of cockerels is regularly practiced to make capons. The capon has all the characteristics of the male and its feathers may be even longer than those of the normal male. The comb, however, remains undeveloped, or, if already large, it dwindles to a fraction of its original size. Here removal of the "reproductive gland" does not change the characteristic plumage of the male, but does change the comb in the direction of the condition found in the hen.

There is one race of domestic fowls in which the cock is hen-feathered. The Sebright Bantam male, Fig. 1 A, differs from

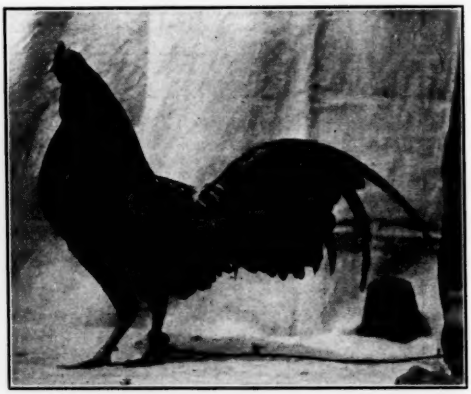


Fig. 2. Sebright Bantam male, after castration, showing cock-feathering.

the ordinary cock in that his feathers are like those of the hen, Fig. 1, B. Both sexes have golden feathers with a black margin. The most striking feature of the plumage of the Sebright male is that the feathers of the back and rump are rounded at the tip and lack the peculiar hackles of the ordinary cock. This resemblance of the male Sebright to the female suggested to me the possibility that if his testes were removed he might change as does the hen when her ovary is removed. In a word, he might become cock-feathered. I carried out some experiments of this kind in 1915, and the results have been fully described in one of the Carnegie Publications (No. 285, 1919). The result of the operation was most striking. As the new feathers came in, it was at once obvious that they were like those of the ordinary cock

bird. When the complete moult had taken place the birds appeared as shown in Fig. 2. The castrated male was now a rich orange color above; the black margin of the feathers over the whole dorsal surface had disappeared; the back and saddle feathers were long and pointed as were those of the neck also. All of these had the characteristic hackles at their outer margins. The tail was now covered with long yellow tail coverts, that are not present in this form in the hen-feathered male.

On the under surface of the castrated males the changes were much less, although the golden centers of the feathers had become darker. The comb and wattles diminished until they

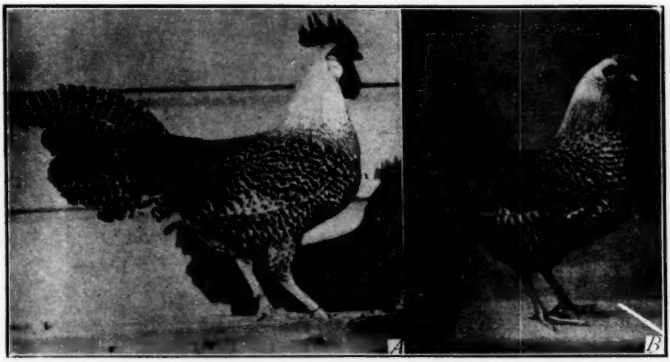


Fig. 3. A. Campine male, hen-feathered; B. Campine female.

were no larger than those of the hen. The effect is the same as in the true capon. Thus results confirmed expectation; the hen-feathered male changed after castration into a cock-feathered bird so far as the plumage was concerned.

There are a few races of poultry in which both hen-feathered and cock-feathered males exist. The Campines have two such kinds of males. In some countries one type is the standard; in other countries the other type. It is more difficult to make from a mixed race a type pure for hen-feathering than one pure for cock-feathering, since the former is a dominant Mendelian character and may carry, but not show, the recessive cock-feathered factor. For the purpose of my experiment it was necessary to obtain a race pure for hen-feathering, and this I succeeded in finding.

The feathers of the hen-feathered male, Fig. 3 A, are barred (except those of the neck) and are like those of the hen, Fig. 3 B. In the cock-feathered male on the contrary the feathers of the back and rump are white and pointed, while the tail coverts are black and long.

When a young cockerel of a hen-feathered breed is castrated he changes over, (Fig 4), as his new feathers come in, until finally he is exactly like the cock-feathered male. His neck feathers become very long and become completely white. The back and rump feathers lose their barring and become white, very long and pointed, and show well developed hackles at the margins. In

Fig. 4. Campine male, castrated, showing cock-feathering.

a word, the hen-feathered male comes to resemble the other type of male. The comb and the wattles, however, remain small as in ordinary capons. Concerning the source of the internal secretion that is probably involved in these changes, the following histological facts are of great interest. In the ovary of the hen there are groups of interstitial cells, called luteal cells (Fig. 5). They are large, clear cells in ordinary preparations, but are found to be filled with granules when methods of preparation are used that avoid the loss of this material. In the adult cock-feathered males these cells are entirely absent as a rule, or at best only sparsely found, and then with shrunken nuclei. In the Sebright cock and in the hen-feathered Campine large numbers of such cells, filled with materials, are present (Figs. 2, 3, 4). In the

hen these cells may be supposed to produce an internal secretion that affects the development of her plumage in such a way that it never shows its complete possibilities. When her ovary is removed this secretion is no longer produced, and she then develops her full plumage, which is the same as that of the male of her race. In the male Sebright and in the hen-feathered Campine the internal secretion produced by their luteal cells may be supposed to suppress in them also the full development of the plumage, but when they are castrated the cells are removed and cock-feathering develops.

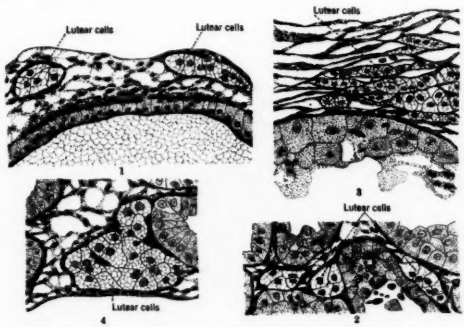


Fig. 5. Lutear cells; 1, in hen's ovary; 2, 3, 4, in testes of Sebright and hen-feathered Campine cocks.

In young chicks of ordinary breeds, the luteal cells are present, both in the males and in the females. This holds also for the young Sebrights as Dr. J. F. Nonidez has recently found. These cells disappear largely or entirely in ordinary breeds, as the birds reach maturity; but in the races with hen-feathering they continue to develop, and remain functional, producing in the males the same effects as they do in the hen of all breeds. The development of the comb and wattles of the male is dependent on the presence of the testes, but it appears that the luteal cells are not directly responsible for their development, because the comb of the hen is small. Some other part or tissue of the ovary and of the testes must be involved in the development of these organs.

ABSTRACT

SOME CONDITIONS AFFECTING THYROID ACTIVITY

W. B. Cannon and P. E. Smith

(1) Gentle massage of the thyroid gland in the cat for two or three minutes will cause an increased rate of the denervated heart amounting in some instances to 33 per cent. over the basal rate.

(2) Massage of another gland, e. g., the submaxillary, does not cause this effect.

(3) The augmentation of heart rate caused by thyroid massage occurs in the absence of the adrenal glands.

(4) Stimulation of the cervical sympathetic trunk as it leaves the stellate ganglia induces a similar augmentation of the rate of the denervated heart; this does not occur if the thyroid gland has previously been removed.

(5) If the cardiac fibres from the stellate ganglia are severed, as well as the vagus nerves, and an afferent nerve such as the sciatic or brachial is stimulated, under such a degree of anesthesia as will permit reflex retraction of the nictitating membrane and dilation of the pupil, there is a primary increase of rate, due to adrenal discharge, which is followed by the slowly developed increase characteristic of the thyroid effect.

(6) If the vagi and the cardiac fibres of the stellate are cut and the animal is asphyxiated under conditions which permit the eye changes described above, there is a similar primary rise due to adrenal secretion followed by the secondary thyroid effect.

(7) If the thyroid glands have been previously removed, sensory stimulation and asphyxia induce solely the increase of rate due to adrenal discharge. The development of the maximal increase of rate from thyroid activity, usually requires from 30 to 60 minutes and passes off in a similarly slow manner.

---

*Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

PHARMACODYNAMIC SUBEPIDERMAL TESTS: II, INDIRECT TESTS; A, THYROIDIN

M. Ascoli and A. Fagiuoli
(From the Institute of Internal Medicine, University of Catania, Director, Prof. M. Ascoli)[1]

A series of investigations is being undertaken in our Institute in an endeavor to ascertain to what extent the intracutaneous injections of endocrin substances and those especially related to the autonomic nervous system can be utilized in practical diagnosis. In a previous issue of this Journal, the results secured with pituitrin were briefly described (2).

The desirability of investigating thyroid material in this way was obvious although it seemed, a priori, less promising on account of our inability to utilize a definitely identified, pure active principle.

As compared with a control subepidermal injection of water, that of thyroid extract differs in giving rise to a larger papule and a greater degree and duration of erythema. The reaction was found to vary a great deal with the individual, however, being now more active and lasting, now so attenuated as to become indistinguishable from the control reaction. But the same variability in the reaction picture is seen following injections made in a given subject at the same time with other extracts, e. g., of ovary, thymus or testicle. The problem does not seem to lend itself, therefore, to a simple, direct attack. Can it be solved by *indirect* methods?

Among the different endocrin organs there are close relationships of interdependence, synergy or antagonism. In the case of adrenalin and pituitrin, characteristic reactions are directly attainable by means of subepidermal injections. In case of other endocrin organ extracts, as above mentioned, unequivocal reactions are not readily secured. The problem then presents itself: Can the adrenalin reaction be characteristically altered—attenuated or accentuated—by the use of extracts of different endocrin organs? The sensitivity of the organism to such materials might thus be disclosed. As a case in point, does the addition of thyroid extract in a quantity not in itself causing reaction lead to augmentation or attenuation of the adrenalin cutaneous re-

action as it has been reported by Falta to affect the metabolic reaction and by Oswald and others to affect the vasomotor reaction?

The test has given positive results in certain pathological but not in normal subjects (3). A given individual reacts distinctly to adrenalin in 1:200,000 dilution, but only feebly to 1:1,000,000. If to the adrenalin in these dilutions a small quantity of thyroid extract (0.01 to 0.005 cc.) be added (4)—a quantity which in itself gives no direct reaction distinguishable from that to distilled water,—*the adrenalin reaction is distinctly enhanced and more protracted,* as compared with the reaction to the adrenalin alone. The central red color in the reacting zone is also often deeper.

The same activation may be demonstrated in case of pituitrin instead of adrenalin and *this second indirect test may be found in cases in which the former is negative* (5).

Contrary to the results obtained with thyroid extract, other endocrin glands seem to attenuate the adrenalin reaction. We shall have occasion to report further upon these latter extracts as well as upon the clinical significance of the indirect *thyroidin test.*

1. Submitted to the Reale Accademia dei Lincei, Rome, March, 1920.

2. Ascoli, M. and Fagiuoli, A.: Pituitrin test. This Journal, 1920, **4,** 33-36.

3. It is presumed that the failure to obtain the phenomenon in the normal subject is due to the insufficient amount of active material in the thyroid extract employed. The result was the same, however, with Oswald's thyreoglobulin.

4. The extracts employed by us are of 25 per cent strength in physiological saline solution, obtained from bovine thyroids under a pressure of 350-400 atm. to the sq. cm. The extract is filtered through porcelain, preserved with ½ per cent chloretone and distributed in sterilized vials. For this preparation we are indebted to the "Instituo nazionale medico farmacologico" of Rome.

5. We have frequently alluded to the necessity of making the injections superficially and strictly subepidermically. This condition is all the more essential in the thyroidin test in whch are to be compared only differences in *intensity* of reactions of the same category such as could readily be produced merely by variations in the depth of the injections. In order to obviate error when differences are small, the test may be made in duplicate or triplicate and be regarded as positive only when the result is obvious and the difference easily appreciable to one not concerned in the result.

STUDIES ON DISORDERS OF THE THYROID GLAND

HYPERSENSITIVENESS TEST WITH ESPECIAL REFERENCE TO "DIFFUSE ADENOMATOSIS" OF THE THYROID GLAND.*

Emil Goetsch, M. D., Brooklyn, N. Y.

Further experiences with my epinephrin hypersensitiveness test during the past year have led to a more intensive study of the so-called border-line cases. In these is found the familiar syndrome of asthenia, loss of weight and strength, nervousness of varying degrees, labile pulse, mild tachycardia, perspiration and tremor, sometimes depressions, and often slight elevation of temperature without, however, any special gross pathological findings in the thyroid gland on physical examination, and without positive eye changes such as are found in exophthalmic goitre. The diagnosis in these instances lies largely between mild chronic hyperthyroidism, incipient tuberculosis, neurocirculatory asthenia, effort syndrome, psychasthenia, psychoneurosis, neurasthenia and other allied nervous states or perhaps even certain chronic infections, for it seems possible that a syndrome of this character, if not actually caused by infection, may be made worse by it. In a series of these individuals most of whom had been suspected of having tuberculosis, while others were thought at first to have psychoneurosis or neurasthenia, and who had failed to improve after the ordinary medical and hygienic measures, there was finally obtained a positive epinephrin hypersensitiveness test which is so characteristic of hyperthyroidism, though, to be sure, not absolutely pathognomonic of it. Because of the failure of the ordinary medical and hygienic measures in the treatment of these individuals,—at Saranac Lake and other sanatoria; because, further, in those suspected of having tuberculosis, little or no tuberculosis was found upon expert examination; because in all there was a fairly uniform syndrome which resembled mild hyperthyroidism and, lastly,

*Read at the Fourth Annual Session of the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

because of a positive epinephrin test, which is negative in pure tuberculosis, I felt justified in advising operation. This consisted usually in a bilateral partial resection of the thyroid gland. In view of the improvement following operation, and because of the characteristic change in the glandular histology, I felt that these cases formed a special and interesting group in thyroid disorders, exhibiting a new clinico-pathological syndrome which deserved reporting, in the hope that more interest and study be awakened in it.

Upon careful histological study of the thyroid gland removed in these cases I found a rather characteristic and striking pathological change which has heretofore escaped general notice, and to which I have applied the name, "Diffuse Adenomatosis." It is my purpose in this report to speak in somewhat greater detail with regard to the importance of this condition in the etiology of latent hyperthyroidism and with regard to its differentiation from incipient tuberculosis and other conditions with allied syndromy, by means of my epinephrin test. I shall speak also of the very definite improvement which follows thyroid resection and of the gross and microscopic pathological changes occurring in the thyroid gland.

It may be well to review briefly our knowledge of the histological changes which occur in the thyroid gland and which are associated with a definite, now well-recognized hyperthyroidism. Thus it is well to remember that the parenchymal, or in other words, the epithelial thyroid cells occur as two types: first, the acinar or aveolar cells surrounding the characteristic colloid and second, the so-called foetal or interstitial cells occurring in the interstices between the normal acini, but not taking part in the formation of the latter. Primary hypertrophy and hyperplasia of the aveolar epithelium, when mild, gives rise to a mild hyperthyroidism, such as is found associated with the hyperplastic thyroid gland at puberty or at other physiological periods, such as pregnancy and menstruation. More advanced aveolar parenchymal hypertrophy and hyperplasia is associated with the higher degrees of thyroid intoxication, and is found in the characteristic gland of exophthalmic goitre or Graves' disease.

The second well-recognized syndrome of hyperthyroidism depends upon the activity of the so-called "foetal-adenomata"

which occur as discreet circumscribed tumors or nodules which may be single or multiple and which are easily recognized, even in the very early stages. There is good reason for believing that these adenomata arise by hyperplasia and overgrowth of individual groups of the so-called foetal interstitial cells of Wölfler, and thus develop into the discreet, circumscribed and encapsulated foetal adenomata. I wish to emphasize here that there is not in the case of true adenoma a general overgrowth of this interstitial tissue in the thyroid gland, for upon this distinction rests the point of my paper. In both these instances of aveolar hyperplasia, namely, in the active gland at puberty and in exophthalmic goitre, I have found, upon cytological study, evidence of cellular activity in the occurrence of great numbers of mitochondria in the cytoplasm of the cells. I reported these findings in the Johns Hopkins Bulletin, May, 1916, and stated further that I felt I had proved from histological evidence that foetal adenomata of the thyroid were of themselves responsible for the hyperthyroidism which occurred associated with them. Furthermore, in both of these clinical states, I found that the epinephrin hypersensitiveness test was definitely positive, and the degree of reaction was remarkably parallel to the degree of toxicity clinically recognizable. The test gave thus confirmatory evidence of the presence of hyperthyroidism in these two conditions.

Before proceeding to a further discussion of the cases to be reported, it may be well to make a preliminary statement as to what the test really means, after my experience with it and after the experience of others. In the first place, it is an indicator of hypersensitiveness of the sympathetic nervous system. On the other hand, I am not prepared to say that all cases which show a positive reaction are, therefore, hyperthyroidism. However, we do know that the test is positive in all cases of hyperthyroidism, a fact which is founded upon abundant physiological research carried out particularly by Cannon and Levy. Furthermore, of all the diseases which may possibly be associated with a hypersensitive sympathetic system, hyperthyroidism is by all odds the most common, the exceptions being relatively uncommon. On the other hand, in the presence of a negative response to the test, one can state definitely, I believe, that hyperthyroidism is not present. To be able to differentiate to this extent is of great value in the diagnosis of obscure cases.

Again, I wish to point out that I am not advocating operation simply on the basis of a positive reaction; I am simply stating the facts as we know them with regard to the test, regardless for the present, of treatment advised.

The reaction is regarded as mildly positive when, after the injection of 0.5 cc. of 1 to 1000 epinephrin chloride (Adrenalin chloride, Parke, Davis & Co.) solution a rise of about 10 points in pulse or in systolic pressure or in both is obtained, and in which there are associated with this, certain clear-cut subjective and objective symptoms which have been described. It is stated by some that, exceptionally, positive reactions are obtained in cases of effort syndrome and even in so-called normal individuals and in neurasthenics. The response in such cases, however, is often atypical. A typical reaction is characteristically sustained and is apt to occur in two phases, a primary major reaction followed by a secondary minor reaction; it then disappears in one and one-half hours, leaving the patient practically normal. Again, the reaction is parallel to the degree of toxicity clinically recognizable just as is the metabolic reaction in the higher degrees of toxicity. After operation or after subsidence of the hyperthyroid symptoms, there is a fairly rapid subsidence of the characteristic hypersensitiveness.

Armed with these facts, I proceeded to a study of the less obvious cases which presented an obscure, though characteristic, syndrome, with negative eye signs and with few diagnostic findings in the gland. Many of the subjects were suspected of having tuberculosis, but upon expert examination were found to have little or none and showed no definite improvement after prolonged periods of rest. Finally, a positive epinephrin test was obtained and, after the failure of other measures, operation was advised. I wish to report now the results after operation and the pathological findings in the thyroid gland.

Space is not available in this brief report for a detailed presentation and discussion of the cases in this series. I shall, therefore, restrict my remarks to a summarized statement. There are in this group fifteen patients suffering with what I have called "Diffuse Adenomatosis" and presenting in general the syndrome of asthenia, mild tachycardia, nervousness, loss of weight and strength, tremor, perspiration and, in most of the cases, slight elevation of temperature. The majority of the

cases were observed during the past year at the Johns Hopkins Hospital and a few of the more recent cases at The Long Island College Hospital. Reports since operation have been obtained in all cases except two, and the time elapsed since operation varies from three to twelve months. The type of operation was the same in all instances, namely, a generous resection of both lobes together with the isthmus, leaving possibly one-fourth of the total gland substance. It seemed necessary to make this extensive reduction in order to obtain the desired benefit.

I may mention now, for convenience of consideration, the sub-groups of this series of patients, according to their previous suspected diagnosis and their previous treatment. The larger group, and perhaps the most interesting one, comprises ten patients in whom the diagnosis of tuberculosis was suspected, and all of whom had the benefit of sanatorium treatment and, incidentally, of expert pulmonary examination. The period of hygienic treatment varied from about three months of sanatorium treatment to irregular periods covering five years. In no case was there sufficient benefit from this treatment to warrant further rest or even to indicate that tuberculosis was the cause of the symptoms. The clinical syndrome in all of these cases is much the same and consists of the symptoms mentioned above. The individual cases did not vary sufficiently to warrant special discussion. The interesting feature about these patients is that upon expert pulmonary examination there was little or no tuberculosis found, and in all cases the epinephrin chloride test was positive, both at the sanatoria where the tests were carried out, and subsequently in the hospital under my own observation. In view of the fact that these patients failed to improve under medical and hygienic measures after long periods of time, that their syndromy seemed to be that of hyperthyroidism even more so than of other conditions which might give a more or less positive epinephrin response, such as diabetes, effort syndrome, neuro-circulatory asthenia, but which could be largely excluded by history and examination; and, finally, because of the positive epinephrin chloride test which has been found so constantly positive in the presence of hyperthyroidism, I did a partial thyroidectomy.

With regard to the clinical results following operation, I might say that I have reports from all but one of the cases, and

although the time elapsed since operation is hardly sufficient as yet to expect all the improvement that I think will come, nevertheless, after the comparatively short post-operative periods of three to twelve months, the results are so encouraging as to make me very hopeful about the ultimate outcome. In only one case was there failure of definite improvement, at least of the mental symptoms of which this patient suffered; physically she has definitely improved. The remaining patients showed a moderate to very remarkable improvement. The symptoms specifically reported as relieved are nervousness, weakness, palpitation, tremor, insomnia, perspiration, loss of weight and the mild febrile condition. These answers were in response to a definite questionnaire sent to these patients. Of the remaining cases of the previously suspected tuberculosis group there were five. One of these was a paraysmal tachycardia case referred to me by Dr. Barker; another, a young woman suffering with weakness, nervousness, and tremor, of unknown origin; the remainder complained primarily of nervousness and weakness.

In the gross and microscopic study of the thyroid glands from these patients I found some peculiarities which have lead me to think that we are dealing with a new clinico-pathological syndrome in thyroid disorders, which is a true hyperthyroidism based upon a peculiar and very interesting pathological change in the thyroid gland. This change is neither of the nature of that found in puberty hyperplasia nor in Graves' disease or exophthalmic goitre, nor is it of the type in which true discreet encapsulated nodules, the so-called "foetal-adenomata," are found. The glandular pathology in these latter types of thyroid disorder is readily recognized and is well known to be capable of producing hyperthyroidism. However, in this new and obscure group of which I am speaking, the following characteristics are fairly uniform. Upon physical examination the thyroid gland is often found moderately enlarged, but may be neither visibly or palpably so. It is fairly firm, and slightly granular or lobulated. No definite nodules are palpable, and signs of increased vascularity such as thrills or bruits in the gland or at the poles are not demonstrable. At operation one characteristically finds that a peculiar periglandular fibrosis has caused the gland to become loosely or sometimes quite firmly adherent by its thickened capsule to the prethyroid muscles and to the

large vessels and the sternomastoid, laterally. The appearance reminds one of a possible mild periglandular reaction, which sometimes makes difficult the delivery of the thyroid lobe. There is increased vascularity, particularly of a venous character, in the capsule of the gland. The thyroid arteries are only slightly if at all enlarged. The gland contains a moderate amount of colloid. It is of "rubbery" or spongy consistence, friable, more than normally vascular and has a marked tendency to ooze from the cut surface. There is not the familiar increased consistence of the gland as seen in exophthalmic goitre, nor is there the glistening character seen in colloid glands.

The microscopic findings are fairly uniform in these glands. The most characteristic feature is the readily recognizable increase in the interstitial cells the so-called foetal cells which are themselves characterized by being without any very definite arrangement. They are large and have a fairly clear protoplasm and a round vesicular nucleus. They can be distinguished from the lymphoid cell accumulations, which are also common, by the fact that the latter cells are much smaller, have very little protoplasm and a dense pycnotic nucleus. This interstitial tissue is distributed throughout the gland substance and is nowhere aggregated into encapsulated nodules as one sees in true adenoma. The glandular acini are mostly small and irregular in size. One sees often numbers of very small acini in the midst of, and apparently derived from, the interstitial tissue, and appearing in cross-section like a globule of colloid surrounded by 10 or 12 cells. The acinar cells themselves are usually low, thinned out and do not of themselves appear active nor are they active as indicated by the presence of mitochondria which are usually very few or practically absent. In other words, the hyperthyroidism which occurs with this change in the thyroid is not due to an increased activity of the acinar cells. In this respect the acinar cells differ from those seen either in the normal gland where they are cuboidal or in the puberty hyperplastic gland or in exophthalmic goitre, in which they are cuboidal to columnar and rich in protoplasm containing abundant mitochondria. Occasionally very small young adenomata are seen no larger than a wheat grain, but this is exceptional. These very small adenomata may possibly be regarded as an index of the fact that the foetal tissue in the thyroid is stimu-

lated to activity and overgrowth by some hidden force. There is some increase in the fibrous tissue which tends to divide the gland into small lobules easily recognized under the microscope. Because of the increased amount of diffuse interstitial tissue which is greater with the more toxic grades of hyperthyroidism found in these cases, and which we believe is derived from the so-called foetal cells of Wölfler; because of the numerous small apparently new formed acini, and the increase in lymphoid cell accumulations; because of the absence of true discreet adenomata and because, finally, of hypoplasia rather than hyperplasia of the alveolar cells, I have, for want of a better term called this condition "Diffuse Adenomatosis." This may not be a very fortunate term, but it has the value of being descriptive. I wish to emphasize again, that the appearance of these glands is decidedly different from that seen in puberty hypertrophy and hyperplasia and in exophthalmic goitre, in which there is a hyperplasia of the alveolar cells and in which the interstitial tissue is almost entirely absent. Furthermore, the picture is very different indeed from that seen in true adenoma, which occurs as an encapsulated tumor in an otherwise fairly normal looking gland.

I believe that the hyperthyroidism in these cases is dependent upon the activity of this so-called interstitial tissue, and not upon the primary alveolar cells, for when applying all the criteria we have in addition to the criterion of mitochondrial concentration, I find that the alveolar cells are more or less thinned out; there is no infolding and when investigated for the presence of mitochondria these latter structures are found very few in number. On the other hand, the interstitial tissue contains a moderate number of these structures, and at times they are quite numerous. In May, 1916, in the Johns Hopkins Bulletin, in an article entitled: "Functional Significance of Mitochondria in Toxic Thyroid Adenomata," I stated that, on the basis of histological evidence in addition to clinical reasons, foetal-adenomata of the thyroid were active and of themselves responsible for the hyperthyroidism associated with them. I believe this to be the case because of the very rich mitochondrial concentration in these adenomata, and because of the almost entire absence of them in the gland outside of the adenoma. Similarly, in puberty hyperplasia and in exophthalmic goitre, these mito-

chondria occur in moderate numbers in the former and are excessively numerous in the latter. This was a uniform finding. In colloid goitres they are very few or entirely absent. In other words, I believe that the hyperthyroidism in these cases is dependent upon the increase in amount and activity of the intersitial tissue derived from the so-called foetal cells and not upon activity of the alveolar or acinar cells themselves.

The question might be asked: Is this syndrome associated with "Diffuse Adenomatosis" a true hyperthyroidism? It might be contended that these persons were by nature endowed with a hypersensitive sympathetic nervous system, and that the operation merely reduces the more or less normal amount of thyroid secretion and thus renders the abnormally sensitive sympathetic less irritable, with a consequent improvement in the status of the patient. This objection might be valid, I think, if the thyroid presented a more normal appearance. But, because of the very definite pathological changes which are found and have hitherto been overlooked as a cause for hyperthyroidism; second, because of the fact that these patients failed to respond to medical and hygienic measures; third, because of the positive response to the epinephrin test, which is the rule in hyperthyroidism and, finally, because of the definite improvement after thyroid resection, I am of the opinion that we are dealing with a clinical state of mild chronic latent hyperthyroidism which has hitherto escaped notice.

If one were to rely upon the metabolic rate as an index of hyperthyroidism one would not suspect the cases belonging to this group, for as recently pointed out by Woodbury, the metabolic rate in these individuals is not particularly increased; in fact, it may be normal or only very slightly abnormal. A series of these cases were operated on by Webb and a definite improvement followed. I think Woodbury is correct in assuming that, regardless of the normal metabolic rate, these patients were suffering with hyperthyroidism. Consequently, the fact that the metabolic rate is not increased in these individuals does not to my mind indicate that they are not suffering with hyperthyroidism. I want to emphasize particularly that the epinephrin test, which is more sensitive than the metabolic rate determinations, is positive in these individuals, though mildly so, and hence is in this group of more diagnostic value than the met-

abolic test. This finding is somewhat similar to that in adenoma in which Woodbury also found that in the quiescent phase the metabolic rate may be found normal, and one would certainly not deny the presence of hyperthyroidism when the clinical syndrome is so clear, and when true circumscribed adenomata are felt in the thyroid gland and discovered at operation. In other words, the hypersensitiveness of the sympathetic is rather a persistent characteristic even in the quiescent phase of hyperthyroidism at which time the metabolic rate is normal. The basal metabolic level, therefore, is not so much an indicator of the disease as an expression of the degree of toxicity which is at any one moment present.

I think we are safe in saying on the basis of the physiological researches of Cannon and his associates, and of my results in the study of thyroid disease during the past six years, that epinephrin chloride is an indicator of hypersensitiveness of the sympathetic nervous system; that of all the diseases which are characterized by such a hypersensitive nervous system, hyperthyroidism is by far the most important and the one most frequently encountered. It would seem impossible for hypersecretion of the thyroid to be present in an organism without producing a hypersensitiveness of the nervous system and, therefore, a positive reaction to epinephrin. On the contrary, given a negative reaction, I feel that one can say definitely that hyperthyroidism is not present except in those late stages in which nervous and cardio-vascular degeneration have so far advanced as to render impossible a response to the drug. A negative reaction is thus of great diagnostic value. A typical positive reaction in a condition from which diabetes, neuro-circulatory asthenia and effort syndrome have been excluded—and this can often be done by other clinical methods—has a distinct diagnostic value, and at other times is confirmatory of a clinical diagnosis based upon ordinary observations and tests.

As compared with the increased metabolic rate as a criterion of thyroid intoxication, I think the test has, in the first place, the distinct advantage of being simpler and less liable to erroneous interpretation. With ordinary care it can be used by any one familiar with a blood pressure apparatus and the observation of cardio-vascular changes and with the general symptoms and signs of hyperthyroidism. It does not require the trained ex-

pert to obtain correct observations nor to make the proper interpretations. Again, in the milder states of hyperthyroidism in which the metabolic rate may be normal or only slightly increased, cases of which kind may thus be overlooked if reliance is placed upon increased metabolic rate alone, a positive epinephrin test often reveals the diagnosis. Again, observers have reported definite instances of clinical hyperthyroidism in which the metabolic rate is low. I have never seen a case of definite hyperthyroidism, clinically easily recognizable, which has failed to give a positive epinephrin test. This has been found true in a series of over 450 cases of thyroid disease. In my experience I think I have been able to differentiate the cases of neuro-circulatory asthenia so-called, which have given a more or less typical reaction, from hyperthyroidism by the fact that, in the former, there is very frequently a clear family history of nervous instability. There is an inherited constitutionally inferior nervous system. The symptoms in this condition are rather obscure and indefinite and upon closer examination it is found difficult for the patient to describe them clearly. They are found to date back to puberty or even into childhood, there being no definite recognizable starting point of the trouble. On the other hand there seems always, in my experience, to be a fairly definite starting point for hyperthyroidism. It is rare before puberty and frequently follows acute infections or severe psychic and nervous trauma. It may have its beginning at puberty, after pregnancy or after the menopause, the patient usually recognizing the time when the symptoms begin, whereas, previous to this time the general health may have been, and often has been, unusually good. Restricted to the epinephrin test alone one might have some doubt. Since it appears that a positive test may be found in the condition of so-called neuro-circulatory asthenia—which to my mind has not been demonstrated to be absolutely unassociated with thyroid overactivity—it may be helpful if this simple history test is applied, for in many cases a differentiation can thus be made from true hyperthyroidism. Again, I want to emphasize that I do not feel or say that in the presence of a positive reaction, particularly a mildly positive reaction, thyroid resection is indicated. I am speaking now simply of diagnostic facts, leaving the matter of operative therapy out of the problem.

SUMMARY

There is a group of so-called borderline cases which heretofore have been very difficult of diagnosis, and even more difficult with reference to a satisfactory treatment. The individuals belonging to this group are of no characteristic age but are mostly young adults. They present a syndrome characteristic of possibly hyperthyroidism, incipient tuberculosis, neuro-circulatory asthenia and allied conditions. They fail to show positive eye signs, or even positive clinical findings in the thyroid gland. They fail, furthermore, to respond to ordinary medical and hygienic measures. Upon further examination they are found to give a positive reaction to the epinephrin test, but on the other hand, as shown by Woodbury, in many instances they fail to show increased basal metabolism. In this type of case a rather extensive bilateral partial resection of the thyroid gland is followed by a very definite and often striking improvement. The thyroid gland upon microscopic examination shows a characteristic histological picture, heretofore unrecognized as responsible for a definite kind and type of hyperthyroidism. This change is not of the puberty hyperplastic type nor of the exophthalmic type, nor is the picture that presented by the well known discreet adenomata of the thyroid gland, all of which conditions are well known to be responsible for hyperthyroidism. In the group of patients reported here the change in the gland consists primarily in a definite and, at times, very marked increase in the interstitial so-called adenomatous tissue, together with increased amounts of lymphoid tissue and an associated hypoplasia of the primary alveolar or acinar epithelium. This interstitial tissue is not aggregated into nodules, but is scattered diffusely throughout the gland. This increase in interstitial tissue is not associated with aveolar hyperplasia, as seen in the puberty hyperplastic gland and exophthalmic goitre, but rather as stated with aveolar hypoplasia. It arises, doubtless, from the interstitial cells; produces a picture finally to which I have given the name of "Diffuse Adenomatosis," and which is capable of producing mild to moderate states of chronic hyperthyroidism. It is my opinion that this is a definite pathological-clinical entity, in fact a new type of hyperthyroid syndrome depending upon a new conception of pathological change in the thyroid.

The fact that this change is responsible for hyperthyroidism to my mind is shown by the fact, that in the first place there

is an associated syndrome produced which is more or less characteristic of the hyperthyroid state; second, there is a failure to improve under the ordinary medical and hygienic measures which are directed to the treatment of similar nervous conditions; third, there is a positive reaction to the epinephrin chloride test; fourth, after resection of the thyroid there is a diminution if not disappearance of this hypersensitiveness with a considerable improvement, in fact, almost a cure in some cases; and fifth, in the gland there are found changes which are characteristic and very different from the normal appearing gland, and very different also from the other well known pathological changes in the thyroid. Should one feel that these cases are not hyperthyroid there still remain to be explained the rather typical symptomatology, the positive epinephrin chloride test, the improvement after operation, and the very characteristic changes in the gland upon microscopic examination.

In conclusion, I wish to state that I do not hold that the epinephrin chloride test is pathognomonic of hyperthyroid states. I would say, however, that a negative test excludes hyperthyroidism, that in all except a few very severe cases of hyperthyroidism the test is positive and that there are some few conditions which give a more or less typical reaction and which are to be remembered as exceptions. The latter I think can be fairly well recognized after a careful history and physical examination. At any rate I feel that the test is practically always confirmatory, in many cases diagnostic, in others suggestive of the diagnosis, and leads to further and more careful search for causes in the small percentage of exceptions to the test. Again, there is a remarkable parallelism between the hypersensitiveness to epinephrin and the degree of hyperthyroidism present. The test is rather easily applied and one can follow the well known variations in the degree of hyperthyroidism present from time to time, and one can regulate the treatment accordingly. I am convinced that when intelligently applied it is of the greatest help in diagnosis, in treatment, and in prognosis, and furthermore, it has led directly to a clearer understanding of an obscure group of cases which, I believe, are dependent for their symptomatology upon a very definite pathological change in the thyroid gland, which has heretofore escaped notice. This change is capable of producing hyperthyroidism, and is different from the well

known pathological histology heretofore described. The condition might well be called "Diffuse Adenomatosis" of the thyroid gland.

BIBLIOGRAPHY

Goetsch, E.: Functional significance of mitochondria in toxic thyroid adenomata. Bull. Johns Hopkins Hosp. (Balt.), 1916, **27**, 129-132

Cannon, W. B. and Cattell, McK.: Studies on the conditions of activity in endocrine glands. II. The secretory innervation of the thyroid gland. Am. J. Physiol. (Balt.), 1916, **41**, 58-73.

Levy, R. L.: Studies on the conditions of activity in endocrine glands. IV. The effect of thyroid secretion on the pressor action of adrenin. Ibid., 1916, **41**, 492-511.

Woodbury, M. S.: A comparison of methods for determining thyrotoxicosis. J. Am. M. Ass. (Chicago), 1920, **74**, 997-999.

HYPOPITUITARISM

A Case Report

Henry H. Lissner, M. D.

The following case came under observation shortly before the War. Although its interest as bearing upon endocrine physiology and pathology was obvious, it was not possible on account of other imperative duties to devote the time to its study which it otherwise would have received. It is regretted, especially, that data for a detailed report on the cytological features of the pineal and other endocrine organs were not secured.

Family History. F. B. who was 23 months old, September, 1915, was the youngest of four children, one boy of 16 years and twin girls of seven. There is no family history of glandular trouble or diabetes.

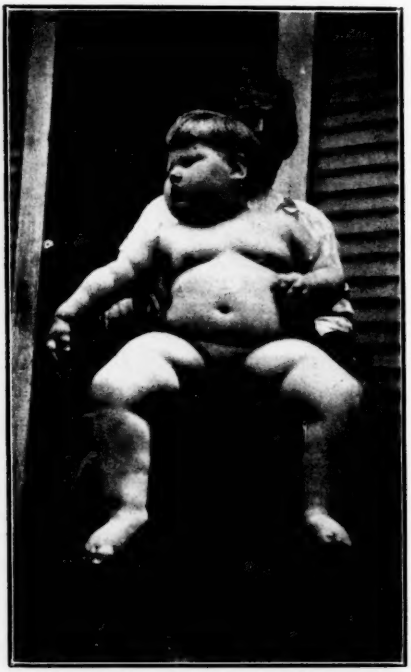
Personal History. The patient's weight at birth was 8½ lbs.; labor was normal; he nursed up to the eleventh month, at which time he was placed on Mellin's food, barley water, and malted milk. He was apparently normal up to the ninth month, laughed, played, noticed what was going on about him and seemed to have a happy disposition. From this time on, it was noticed that he was gaining very rapidly and a photograph at this period shows an early tendency to deposition of fat and the early expression and phases of his condition.

At this time, also, he had his first convulsion and, for a time, at every urination he would close his eyes and fall forward in a convulsive seizure. These convulsions, occurring sometimes as often as seven a day, continued up to the age of fifteen months, when they became more severe in character but still remained of the flexor type. The number of convulsions for sixty-four days from the 15th to the 17th month of his life was 3.6+ spells a day.

Examination. The child has neither walked nor talked and because of his undeveloped condition, we cannot say whether or not certain symptoms which require some mentality for their determination, were present, such as headache, photophobia, and nystagmus. Because of the very thick layer of fat and small size of the blood vessels, the systolic pressure was difficult to

determine. It was found to be about 80. The diastolic pressure was not obtained.

Eyes. Examination of the eyes by Dr. F. K. Miller showed pupils normal and no apparent oculomotor paralysis. The eye-ground showed edema of the retina.



Photograph of subject at the age of 23 months.

Throat. Examination of the throat by Dr. C. H. Montgomery showed: "Tonsils and adenoid present; no bulging of the naso-pharynx; no epistaxis, no cerebro-spinal rhinorrhea."

General Condition. He has, fairly constantly, a pronounced facial cyanosis. Pressure in the anterior fontanelle causes a drawing up of the hands and thighs and an expression of pain and protest, rolling of the eyes, and it would seem that if continued it would bring on a convulsion. There have been

from the onset marked muscular weaknesses and inability to sit up. He makes no effort to help when picked up and falls limply to either side, due no doubt to a muscular dystrophy.

His appearance is very striking: his hair is coarse, light in color, and grows very rapidly; his fingers are puffed and tapering. His head is enormous, breasts are prominent, and there are rolls of fat which make decided creases about the neck, arms, legs and abdomen.

The external genital organs are diminutive. His weight at 15 months was 37¾ lbs.; at 2 yrs., 41¾ lbs.; at 3 yrs., 81 lbs.; practically doubling his weight in his third year. His measurements May 18, 1917 were as follows:

Circumference of head	55½ cm.
Fronto and submental	59 cm.
Chest under the breast	88½ cm.
Abdomen at the umbilicus	96 cm.
Thigh at the gluteal fold	53½ cm.
Calf of leg	30 cm.
Upper arm	27½ cm.
Height	100 cm.

The sugar tolerance test was done. He was given 60 gms. of levulose at 9:00 A. M. The urine secretion of the first hour was 5cc. and the test for levulose, negative. The second hour it was 13 cc. and the test was negative. The third hour secretion was 10cc. with a slight reaction indicating levulose in the urine but following this, there was total suppression up to 11:00 P. M. of the same day, when the kidney function gradually returned.

The convulsions continued very severe up to July, 1917, when he had two spells of explosive vomiting, following which the convulsions ceased. On the same day, he began to run fever between 99 and 101 degrees. His fever continued for one week, during which time it gradually increased up to 103 degrees. He was given small doses of aconite by his mother to reduce the fever and on the 19th, 20th, and 21st of July he was fever free. The fever started again, however, between 102 and 103 degrees, and on the 25th of July, he began groaning and gradually went into coma. The fever increased from 103 to 104 degrees until on the 30th day of July, when he died at 8:00 P. M. with an ante-mortem temperature of 107½ degrees.

Treatment: The treatment, as outlined, was two grains of pituitary extract three times a day. This was gradually increased until he was taking twenty two-grain tablets daily without any apparent benefit. There was no change in the mental development, muscular strength nor genitals. Because of the sudden increase in weight he was given 1/10 gr. thyroid extract three times daily. It seemed, however, to increase the number and severity of convulsions so that on the third day it was discontinued.

Autopsy and report on sections by Dr. Herman Zeiler follow.

Inspection: Body of child which has the appearance of being about seven years of age. Body in rigor mortis, and showed post-mortem discolorations, in the dependent portions. Genitals small; entire body appears puffed, but the pitting is not that of a true edema. Abdomen distended; neck very short; mammae well developed.

Palpation: Fontanelles closed.

Skull: Opening the skull the bones are hard and appear thickened. There is marked edema of the piaarachnoid; dura thickened.

The base shows a small sella with the anterior and posterior clinoid processes under-developed. No separation of sutures at the base. Middle ears are clear; ethmoidal and sphenoidal sinuses are clear.

Pituitary body present and under-developed. Incision of chest and abdomen shows fat of the chest about 2 inches thick, very pale; the layer of abdominal fat being somewhat thicker. No evidence of edema.

The pectoral muscles are thin and undeveloped; the abdominal recti very thin; sterno-cleido-mastoid muscles are thin and underdeveloped as are also the muscles of the legs.

Lungs show hypostatic congestion and a few epipleural hemorrhages.

Heart muscle pale; heart fatty and small; on the right side it shows thin musculation with fair musculature on left side. Valves competent. Thymus almost absent.

Abdomen: Shows pale, fatty omentum and very fat mesentary. The fat in the region of the round ligament, very abundant, being ¾ of an inch in diameter.

Spleen is soft and enlarged.

Liver normal in size and pale.

Intestinal tract normal except for retrocaecal appendix.

Pancreas appears enlarged almost to the size of an adult's.

Tissues Examined Histologically—Thyroid: Shows the usual glandular structure of the thyroid, lined by low columnar epithelium and no excess of fibrous tissue. The blood vessels are fairly numerous. There is no cyst formation of any of the glands and but few show colloid substance.

Testicles: The convoluted tubules are diminished in number and separated by abundant loose connective tissue. The cells lining the convoluted tubules are pale-staining and the nucleoli are well marked. No mitotic figures discovered.

Pancreas: Appears normal.

Spleen: Histologically is practically normal.

Kidneys: No increase in fibrous tissue. The cells lining a few of the convoluted tubules and collecting tubules show hyaline necrosis and an occasional tubule shows eipthelial casts.

Hypophysis: The line of demarcation between anterior and posterior lobes seems lost. Histologically, numerous thin walled blood vessels form a plexus surrounding strands of polyhedral cells arranged in three or four rows. These cells are of the usual two types found in this gland and intermingle without definite arrangement or regularity, the "chief" cells being far more numerous. Here and there are a few follicles lined by low columnar epithelium. There is an abundance of loose connective tissue.

SUMMARY

A child of 23 months was normal to the 9th month, when he began gaining rapidly in weight. The onset of symptoms was convulsions of the flexor type continuing up to within the month of his death. The family history showed no glandular trouble or diabetes. The eyes showed edema of the retina; the throat was negative. There was marked muscular dystrophy with profound facial cyanosis, diminutive external genitals, doubling of weight in the third year of life, low sugar tolerance and ante-mortem temperature of 107½ degrees. Treatment consisted of pituitary extract—whole gland—from 2 to 40 grains daily without any benefit. Thyroid extract seemed to irritate. X-ray plates of the skull showed a small sella turcica at the age of 23 months. An autopsy report and the histological report on various glands are included.

THE EFFECTS OF INANITION UPON THE ADRENAL BODIES—PRELIMINARY COMMUNICATION

Swale Vincent and M. S. Hollenberg

(From the Physiological Laboratory, University of Manitoba, Winnipeg, Canada)

It must be admitted that it is still impossible to give a definite answer to the question, "What is the function, or what are the functions, of the adrenal bodies?"

Several important facts have been made out and some theories have been put forward. The facts are:

I. A definite chemical substance of known composition and possessing well marked pharmacodynamical activities can be extracted from the chromaphil tissues.

II. This substance, adrenin, can be obtained from adrenal medulla as well as from chromaphil tissues in other situations.

III. There is considerable evidence that adrenin is actually poured out into the circulation.

IV. The true adrenal body or cortex is related in some way to the development and growth of the sex organs.

The chief theories of modern times in regard to the functions of the glands apply only to the chromaphil tissue. It has been supposed that adrenin is continuously poured out and exercises a tonic influence upon the sympathetically innervated organs and tissues and so, for example, helps in maintaining the normal blood pressure. This theory has been generally abandoned. A more recent view is that the secretion of adrenin is of service only in certain physiological emergencies. The latter suggestion is certainly a more plausible one than the former, though it cannot be said to be firmly established.

The conception has been formulated that the thyroid and adrenal bodies form part of a mechanism for the chemical heat regulation of the body, and that the cortical adrenal and the chromaphil tissue both take part in this functional activity. This theory involves the conception of a widely reaching influence of the adrenal bodies, taken as a whole, upon the metabolism of the organism.

Recently McCarrison (1) has made the important discovery that in pigeons inanition gives rise to a remarkable enlargement of the adrenals. He remarks that, "This enlargement appears to be a true hypertrophy, since it is associated with a corresponding increase in the glands' content of the medullary secretion, adrenalin." It would appear from this quotation that McCarrison regards the cortex and medulla as constituting one gland whose whole function is the secretion of adrenin.

We have repeated McCarrison's experiments upon pigeons, and have also carried out similar experiments upon rats and dogs. We are able to confirm fully his observation that after a period of inanition there is always a distinct hypertrophy of the adrenal bodies. In pigeons the adrenal bodies are doubled in weight after inanition for 15 days. In dogs after a somewhat longer period of inanition the adrenal bodies are almost double the normal weight. In rats the hypertrophy is considerably greater than in pigeons and dogs, even when inanition is carried out for a shorter period.

We reach, then, the remarkable conclusion that, while the majority of organs and tissues in the body atrophy in starvation, the brain and heart remain unaltered and the adrenal bodies hypertrophy to a considerable degree. We have noted that the abdominal chromaphil body (2) in the dog is markedly increased in dimensions after 14 days' inanition, but the chrome reaction was less intense than in the normal dog. This indicates that, in future investigations, a differentiation will have to be made between hypertrophy of the chromaphil tissue and an increase of its adrenin content.

The question naturally arises, "Have we here to deal with a hypertrophy of the cortex, or of the medulla, or of both?" This point we do not pretend to have settled. McCarrison, as seen above, found the adrenin content increased in his starvation pigeons, though in a later communication (3) he notes a diminution of adrenin content in scorbutic guinea-pigs. It is not clear whether McCarrison regards these differing results as due to varying degrees of starvation, or whether he regards the scorbutic influence as something qualitatively different from the inanition influence. Our own results with inanition animals have not been quite consistent. In some cases the amount of chromaphil tissue and the amount of adrenin have been distinctly in-

creased as a result of inanition. In other cases (and these, contrary to expectation, were those of the longer periods of starvation), the opposite effect has been produced, namely, a reduction in the amount of chromaphil tissue, or in the intensity of its chrome reaction, and a reduction of the adrenin content as shown by the physiological test.

We consider these observations of McCarrison to be of the greatest importance since they demonstrate clearly a relation between the adrenal bodies and the general metabolism of the animal organism. Since other lines of work have so far taught us so little of the uses of the adrenal bodies, we are tempted to urge a vigorous pursuit of investigations bearing upon their metabolic functions.

BIBLIOGRAPHY

1. McCarrison, R.: The pathogenesis of deficiency disease. Indian J. Med. Research (Calcutta), 1919, **6**, 275-355.
2. Vincent, S: The chromaphil tissues and the adrenal medulla. Proc. Roy. Soc., London, 1910, **82**, B, 502.
3. McCarrison, R.: The influence of a scorbutic diet on the adrenal glands. Indian J. Med. Research (Calcutta), 1919, **7**, 188-194.

THE ROLE OF THE ENDOCRINE GLANDS IN CERTAIN MENSTRUAL DISORDERS

WITH SPECIAL REFERENCE TO PRIMARY DYSMENORRHOEA AND FUNCTIONAL UTERINE BLEEDING*

Emil Novak, Baltimore, Md.

(From the Gynecological Department of Johns Hopkins University)

Speaking generally, the importance of the hormone associations of an organ or of a body function varies with the degree of its automaticity. The highly volitional functions, such as the skeletal muscular movements, are under the control of the rapidly acting nerve mechanism, while the auxiliary influence of the endocrine apparatus is relatively slight. With the more primitive vegetative functions the reverse is true, for here the mechanism is usually essentially of the endocrine type, with a greater or less degree of contributory regulating influence on the part of the sympathetic nervous system.

Menstruation is a function which may certainly be classed as vegetative, and hence it is not surprising that the explanation of its mechanism is to be sought chiefly in a study of the functions of certain endocrine glands, and that the cause of menstrual disorders is not infrequently to be found in disorders of these structures. That there is, even in the case of menstruation, some association with the higher centers, is shown by the occasional occurrence of menstrual aberrations under the influence of profound psychic disturbances—the amenorrhea which is often seen in women who dread pregnancy, or in those with an intense longing for it; the occurrence of either amenorrhea or excessive menstruation as a result of sudden shock or fright, etc.

For nearly a hundred years, the ovary has been looked upon as essential to menstruation, but no attempt was made to explain the manner in which its influence is exerted, until the formulation of the well-known theory of Pflueger, in 1865. According to the latter, menstruation was explained as the result of a pelvic hyperemia induced reflexly by the pressure of a growing

*Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

Graafian follicle on the ovarian nerve terminations. This theory was quite universally accepted until it was disproved by the experimental work of Knauer, Marshall and others. These investigators showed that removal of the ovaries, thereby severing all their nerve connections, does not cause cessation of menstruation, provided that the ovaries be transplanted elsewhere into the body. In other words, the ovarian influence is exerted through the blood-stream and not through the nerves, i. e., it is of endocrine nature.

The next step was to determine which of the constituents of the ovary is responsible for the menstrual function. Is it the stroma, the follicles, or the corpus luteum? Without going into detail, suffice it to say that the weight of evidence is overwhelmingly in favor of the view that it is the corpus luteum which plays the most important role in this connection. It seems almost as certain, however, that the ovary produces more than one hormone. Marañón, for example, believes that the ovarian hormones may be divided into three groups: One, the genital, has to do with the menstrual cycle; a second, the sexual, with the morphological sex characteristics and a third, the general, assists in all the body functions.

The internal secretion of the ovary is closely interrelated with that of other endocrine glands, especially the thyroid, pituitary and suprarenal bodies. These relations are not easily defined in the present state of our knowledge, but their existence is demonstrated by the frequent influence exerted on menstruation by disease of any of them. Many interesting examples of these relationships suggest themselves for discussion—the role played by the ovaries in the development of the secondary sex characters; the effects of castration at various ages; the rare occurrence of female eunuchoidism; the relation between menstruation and ovulation, and between menstruation and lactation; the influence on menstruation of the thyroid, pituitary and suprarenal bodies, etc. For the purpose of this brief paper, however, it has seemed more profitable to limit myself to the discussion of two or three of the less obvious relations of the endocrine structures to disorders of menstruation.

First of all, I may pass with mere mention that form of amenorrhea now generally recognized as being due to hypopituitarism, and which, clinically, is commonly associated with obesity.

Fröhlich's report, in 1901, of the first case of adiposo-genital dystrophy, gave rise to much experimental work, which yielded results long since incorporated into clinical practice. Much has been written concerning the amenorrhea which is found in connection with hypopituitarism, and I shall not elaborate on the subject here.

The two menstrual disorders to which I wish to call especial attention, as regards their probable endocrine etiology, are (1) primary or spasmodic dysmenorrhea and (2) uterine hemorrhage of the type commonly spoken of as "idiopathic" or "functional."

Primary Dysmenorrhea. At first thought there would seem to be little connection between primary dysmenorrhea and the endocrine system, and yet I believe that an important relation of this sort does exist. By primary dysmenorrhea we mean that form of menstrual pain which occurs in the entire absence of discoverable disease in the pelvis. It is observed with great frequency in young nulliparous women, either single or married, and, in the aggregate, is the cause of a vast amount of suffering. The factors which have been considered instrumental in the causation of this form of dysmenorrhea may be summarized as follows.

1. *Mechanical obstructions of the uterine canal.* For many years after the publication of the work of Mackintosh in 1832, the view was held that spasmodic dysmenorrhea is always due to mechanical obstruction to the exit of menstrual blood from the uterus. Most commonly, it was assumed, the obstruction is due to anteflexion of the uterus. According to this view, the colicky pain so characteristic of the condition is due to spasmodic contractile efforts on the part of the uterine muscle. This conception is still quite prevalent among medical men, although the evidence is clearly against its correctness. For example, primary dysmenorrhea often occurs in the entire absence of anteflexion or of other obstructive lesions, and, on the other hand, it is not uncommon to find even very sharp anteflexions in women who suffer no dysmenorrhea whatsoever.

2. *Neurotic factor.* Aside from the actual hysterical cases, the importance of this factor lies in the fact that it increases the susceptibility to pain, and thus causes a magnification into actual

pain of the menstrual discomfort normally experienced by many women.

3. *Hypoplasia of the uterus.* There is little doubt that by far the most important factor in the etiology of spasmodic dysmenorrhea is defective development of the uterus. It is extremely common to find a greater or less degree of genital hypoplasia in women whose development otherwise is quite normal. These cases of uterine hypoplasia may be classified under three heads, according to the degree of hypoplasia. (a) In the *fetal type,* the arrested development occurs at a very early stage, so that the uterus resembles that of the fetus. The special characteristics are the small size of the uterus and the fact that it is made up almost entirely of cervix, the corpus uteri being exceedingly rudimentary. (b) In the *infantile type,* the uterus resembles that normally found in infants and young children. Here again the cervix predominates over the corpus, although the latter is not as rudimentary as in the fetal type. The uterus as a whole is larger and there is often an associated anteflexion, most commonly of the cervico-corporeal variety. (c) In the *subpubescent type,* the hypoplasia is relatively slight. Here, also, there is not infrequently an associated anteflexion. For a fuller discussion of these varieties of uterine hypoplasia and of their clinical significance, I would refer to a previous paper which I have published on the subject.

The pertinence of the question of uterine hypoplasia in connection with the present discussion rests on two factors: first, that an extremely frequent symptom of uterine hypoplasia, though not by any means a constant one, is primary or spasmodic dysmenorrhea; secondly, that the underlying cause of the various grades of uterine hypoplasia is undoubtedly of endocrine nature. In searching for a cause for the hypoplasia, we at once make contact with the endocrine apparatus in the body. Which of the endocrine glands is responsible for the defective development of the uterus noted in these cases? In the first place, does the ovary exert any important influence on the development of the uterus before the age of puberty, that is, during the fetal and infantile periods of life? Certainly no such influence can be assigned to the corpora lutea, for the latter do not appear before the age of puberty. The possibility suggests itself that some other element of the ovary may possess this function, but the evidence is not

convincing. Mayer believes that the growth of the uterus in very early life follows the general laws of body growth, and that it is not especially influenced by the ovaries. He believes, for example, that in the exceedingly rare congenital anomaly of absence of both ovaries, the uterus may still be present. With unilateral absence of the ovary, the uterus is usually quite normal, as I observed in a recent case. This observation is, however, of no particular significance when we consider that the ovarian influence is blood-borne, and would, of course, exert its effect equally upon the Müllerian ducts of both sides. Mayer attempted to attack this problem with greater directness by performing castration of the animal fetus in utero. The operation was performed transperitoneally, but, unfortunately, terminated fatally as the result of infection. While, therefore, the predominant influence of the ovary during menstrual life is universally admitted, there is no convincing evidence that it is equally important before this period.

There is much reason to believe that the earlier growth of the uterus is under the influence of other endocrine glands, especially, perhaps, the hypophysis. This seems all the more probable in view of the undeniable role played by the pituitary in the production of acquired sexual hypoplasia. For this there is abundant evidence, both experimental and clinical. It would be rash for those of us whose work is chiefly clinical to offer an explanation of the exact mechanism involved in these cases. The point which I wish to emphasize is merely that this type of menstrual disorder may, with reasonable certainty, be classified as an endocrinopathic manifestation.

Functional Uterine Bleeding. Another gynecological complaint the endocrine origin of which permits of very little doubt is the so-called functional uterine hemorrhage. This symptom is of very frequent occurrence, especially at the two extremes of menstrual life, puberty and the menopause. It may, however, occur at any age. In these cases the most careful examination may show perfectly normal pelvic organs, and yet bleeding may be persistent and perhaps very profuse. Most commonly it takes the form of menorrhagia rather than metrorrhagia. Cases of this type usually come to curettage sooner or later, and indeed, in the case of climacteric hemorrhage, the indication for this procedure is urgent, owing to the importance of excluding carci-

noma. In the non-malignant climacteric cases, and in those of puberty, the pathological report on the curettings has usually been some such designation as "normal endometrium," "hypertrophic glandular endometritis," "chronic endometritis," etc. It has seemed difficult to incriminate the endometrium as the cause of bleeding of this type. Equally unsatisfactory have been the efforts to explain this form of bleeding by such factors as artesiosclerosis of the uterus, the "insufficientia uteri" of Theilhaber, etc. The point which I should like to emphasize is that the endometrium in a very large proportion of these cases—I am not as yet prepared to put it in percentage figures—conforms to the type described by Cullen as hyperplasia of the endometrium.

The histological picture presented by this condition is extremely characteristic. As the term indicates, there is a genuine hyperplasia of the uterine mucosa, with an increase of both the epithelial and stromal elements. Owing to the epithelial proliferation, many of the glands become much enlarged and of cystic appearance. The disparity in the glands is perhaps the most conspicuous feature of this condition apparent on casual examination, so that as a rule the diagnosis may be made almost at a glance. That the cystic condition of the glands is not due to mere retention of the contents is suggested by the fact that the epithelium, instead of being flattened out, is commonly quite intact. Not infrequently the epithelial cells are seen to be several layers thick. The stroma is also markedly increased, and occasionally mitoses are noted. Grossly, the endometrium in these cases is almost always much thickened, sometimes enormously so. In the extreme cases curettage will often bring away large masses of fungoid tissue, which lead to a strong suspicion that a malignant condition exists. In other cases the thickening is relatively slight.

An endometrium of the type above described is never observed except in association with the symptom of uterine bleeding. The reverse is, of course, not true, for uterine hemorrhage may be due to many anatomic causes. With most of the ordinary pelvic lesions the endometrium is perfectly normal. It is of interest, however, to note that with certain pelvic conditions, especially myoma and adenomyoma, the endometrium may exhibit the condition of hyperplasia, as above described. There is some evidence to indicate that both myoma and adenomyoma are due to some as yet unknown aberration of ovarian function and, as we

shall see, there is little doubt that the same factor is responsible for hyperplasia of the endometrium.

The finding, in a case of uterine bleeding, of such a definite structural alteration as hyperplasia of the endometrium, would seem at once to take a case out of the category of functional hemorrhage. There is good reason to believe, however, that this characteristic change in the endometrium does not represent a primary lesion, but that it is secondary to a disturbed function of the ovary. Under normal conditions the endometrium is certainly subordinate to the influence of the ovary. The ever changing histological appearance of the uterine mucosa at different phases of the menstrual cycle is undoubtedly called forth by corresponding cyclical changes occurring in the ovary, and especially in the corpus luteum. So that there is nothing revolutionary in the idea that the characteristic picture of hyperplasia may be associated with some definite endocrine disturbance of the ovary.

Hyperplasia, generally speaking, is observed only during the reproductive life of the woman, that is, during the period of ovarian activity. This fact in itself would suggest some influence on the part of the ovary. Furthermore, curettage, in cases of hyperplasia, is most frequently unsuccessful in the relief of the accompanying hemorrhage, the latter symptom recurring in a large proportion of cases. Were the hyperplasia a local lesion in the endometrium, its removal should be followed by cure. That this is not the case would seem to indicate that the underlying cause, an endocrine disorder of some sort, still remains operative. Although repeated curettage frequently does not cure these cases, radium or the X-ray usually brings about a cessation of the abnormal menstruation, apparently by its destructive action on the follicles of the ovary.

As a matter of fact, there is no little evidence that almost all cases of uterine hemorrhage, with the exception of those due to such destructive lesions as cancer, are functional in the sense that the bleeding is due, in part at least, to disturbances of the ovarian secretion, as a result of the pelvic disease, whether this be myoma, pyosalpinx or some other condition. In other words, the simple congestion caused by these lesions is not in itself sufficient to explain the menstrual excess which is often present, and which is probably due to hyperfunction of the ovary. I shall not review the evidence along this line, but it is so impressive that no

intelligent gynecologist can afford to overlook the importance of the pathological physiology of the ovary in the consideration of possible causes of uterine bleeding.

Efforts have been made to ascertain whether the ovarian disorder is associated with any characteristic histological changes in the ovary. The most recent, and also the most valuable, work along this line is by Schroeder. According to this author, the secretory stage normally exhibited by the endometrium just before menstruation is absent altogether in cases of hyperplasia. In the latter, he concludes from his own studies, there is an absence of active corpora lutea in the ovaries. The hyperplastic endometrium, he believes, represents only a persistence of the proliferative stage which, in turn, is due to the persistence of the maturing Graafian follicles upon which this stage is normally dependent. The work of Schroeder is extremely suggestive but needs further confirmation before it can be accepted. Certainly the absence of the corpora lutea is not, as he says, a constant observation, for a well-marked corpus luteum, in the stage of late vascularization, was found in the ovary of one of my recent cases of hyperplasia.

As to the nature of the endocrinopathy present in these cases, we cannot as yet speak with much definiteness. In view of the excessive menstruation characterizing cases of this type, the natural assumption would seem to be that we are dealing with a hypersecretion of the ovary, or, at any rate, with that element of the ovary concerned with the production of normal menstruation. Since most of us are inclined to assign this role to the corpus luteum, it is not easy to explain the absence of corpora lutea which Schroeder believes to be the characteristic finding in the ovaries of these cases.

Hypersecretion of the ovaries (hyper-oöphorism, female hypergonadism) is a condition concerning which we know far less than we know about female hypogonadism. From what has been said, however, the evidence would seem reasonably complete that hyperplasia of the endometrium is the result of hypersecretion of the ovaries. I know of no other clinical condition concerning which this statement may be made with as much justification.

In this brief paper I have merely touched upon a few of the less obvious relationships which exist between the endocrine apparatus and the mechanism of menstruation. There is, perhaps,

no field in which the study of endocrinology is of such fundamental importance as in that of gynecology. The truth of this statement I trust will be apparent from the foregoing discussion of the etiology of three important menstrual disorders—one of the most common forms of amenorrhea, perhaps the most important type of dysmenorrhea encountered by the gynecologist, and a form of uterine hemorrhage the study of which had previously given rise to many theories, all inadequate.

BIBLIOGRAPHY

Cullen, T. S.: Cancer of the uterus. New York, 1900, p. 479.

——Address in gynecology, Can. Med. Assn. J. (Toronto), 1913, **3,** 658-671.

Fröhlich, A.: Ein Fall von Tumor der Hypophysis Cerebri ohne Akromegalie. Wien. klin. Rundschau, 1901, **15,** 883; 906.

Knauer, E.: Die Ovarientransplantation. Experimentelle Studie. Arch. f. Gynäk. (Berl.), 1900, **70,** 322-376, 3 Tab.

Mackintosh, John: Elements of pathology, and practice of physic. 2nd ed. 2 v, **14,** 554 pp.; **17,** 467 pp. 8° London, 1831.

Marañón, G.: La Edad Critica, Madrid, 1919. (Abst. in Internat. Abst. of Surgery, March, 1920).

Marshall, F. H. A.: The comparative physiology of menstruation and the allied processes. Internat. Clin. (Phila.), 1907, 17 S., **2,** 190-197.

Mayer, August: Uber den Einflusz des Eierstocks auf das Wachstum des Uterus in der Fötalzeit und in der Kindheit und über die Bedeutung des Lebensalters zur Zeit der Kastration. Ztschr. f. Geburtsh. u. Gynäk. (Stuttgart), 1915, **77,** 279-300.

Schröder, R.: Anatomische Studien zur normalen und pathologischen Physiologie des Menstruationszyklus. Arch. f. Gynäk. (Berl.), 1915, **104,** 27-102.

Novak, E.: Infantilism and other hypoplastic conditions of the uterus. J. Am. M. Assn. (Chgo.), 1918, **71,** 1101-1107.

EFFECT OF SUBCUTANEOUS INJECTIONS OF THYMUS SUBSTANCE IN YOUNG RABBITS

Ardrey W. Downs and Nathan B. Eddy
(From the Physiological Laboratory, McGill University, Montreal, Canada)

In a previous paper one of us (N. B. E.) reported the effect on full-grown rabbits of subcutaneous injections of desiccated thymus substance (Armour & Company). The doses administered were 10 mgm. and 20 mgm. per kilogram of body weight dissolved in a mixture of one part of glycerine to four parts of physiological saline solution. For control, other rabbits were injected with the glycerine-saline mixture. Each rabbit received forty injections during a period of eight weeks. At the conclusion of the experiment, half of the rabbits were autopsied. Both control and thymus rabbits gained in weight, the former 18.31 per cent, the latter 17.85 per cent. There was no apparent difference in the behavior of the two groups of animals. At autopsy the thyroid glands of the thymus rabbits averaged slightly heavier, 8.57 per cent, than those of the controls. There were no differences in the other organs.

Before this paper appeared, Olkon reported a series of experiments in which he had injected desiccated thymus gland (Armour & Company) suspended in physiological saline solution intraperitoneally into young guinea-pigs. He found that the injections produced marked loss of weight, muscular spasms and convulsions. As a control he injected into other guinea-pigs desiccated muscle protein. These injections caused similar results but in degree much less marked. He concluded, therefore, that the effect in the first case was a specific toxic action of the thymus substance. However, the doses of thymus substance which he employed were not based on body weight. He does not state the dose of desiccated muscle protein used.

Because of this difference in results, we have performed further experiments in which subcutaneous injections of desiccated thymus substance were administered to young rabbits. Twenty-four animals were used, comprising seven litters of three to five animals each. The rabbits of a litter were kept together and separate from all the others. One or two animals of a litter

served as controls; the others were given the thymus injections. The first four litters (14 rabbits) were six to seven weeks old at the beginning of the experiments; the others were nine to ten weeks old at the beginning. Details of the grouping of the rabbits by litters, their age, sex, etc., are given in Table 1. All were in good condition and apparently normal. The rabbits were fed and cared for under our personal supervision and the diet and environment were as uniform for all as it was possible to obtain.

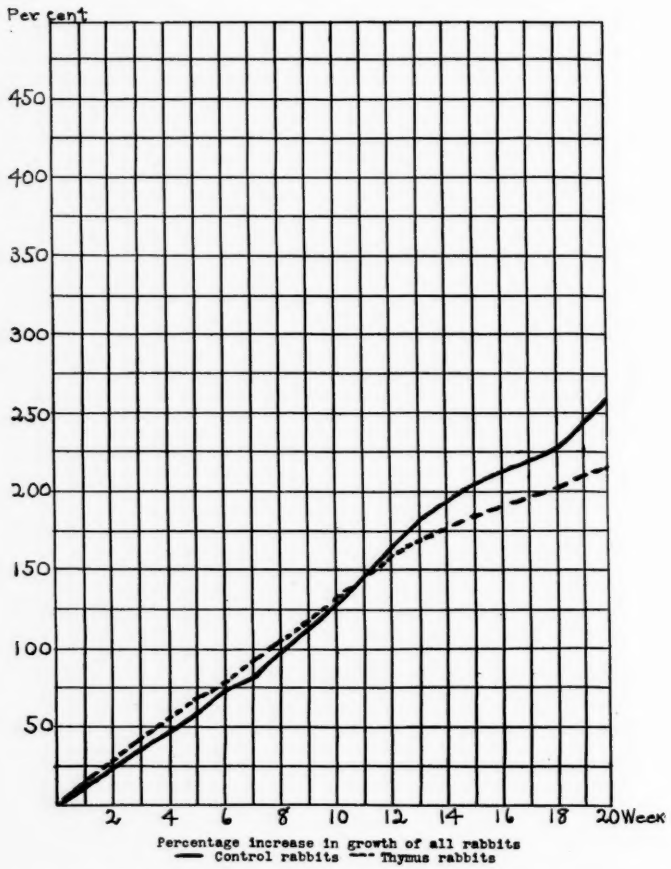
TABLE I

	Number	Litter	Age at beginning weeks	Sex		Genitalia
Group I		A	6	Female	Control	Normal
	2	A	6	Female	Thymus	Normal
		A	6	Female	Thymus	Normal
	4	B	6	Female	Control	Normal
	5	B	6	Male	Thymus	Normal
	6	B	6	Male	Thymus	Normal
	7	C	7	Female	Control	Litter during 20th week; pregnant at autopsy
	8	C	7	Female	Thymus	Pregnant at autopsy
	9	C	7	Male	Thymus	Normal
	10	D	7	Female	Control	Normal
	11	D	7	Male	Control	Normal
	12	D	7	Female	Thymus	Infantile
	13	D	7	Male	Thymus	Normal
	14	D	7	Female	Thymus	Litter during 20th week
Group II	15	E	9	Male	Control	One testicle
	16	E	9	Male	Thymus	Normal (separate from others of litter from 10th week on)
		E	9			
	17	F	9	Female	Thymus	Pregnant at autopsy
	18	F	9	Male	Control	Normal
	19			Male	Thymus	Normal
	20	F	9	Female	Thymus	Normal
	21	G	10	Male	Control	Normal
	22	G	10	Male	Control	Normal
	23	G	10	Male	Thymus	Normal
	24	G	10	Male	Thymus	Normal

As in our previous experiments we used for the injections powdered desiccated thymus gland (Armour & Company) one gram of which is said to represent approximately five grams of fresh thymus gland of the calf. This preparation is but indifferently soluble in water, so that we have found it better to mix the dry powder first with glycerine and then to dilute with physiological saline solution. By this means a satisfactory suspension for hypodermic administration can be obtained. We used one part of glycerine to four parts of saline solution and the final preparation contained twenty milligrams of thymus substance per cubic centimeter. A mixture of one part of glycerine to four parts of saline solution was made for the control injections. The materials were warmed to 37°C. and injected under aseptic precautions. No infection occurred in any of the rabbits, but with the larger doses considerable induration was

produced at the site of injection. The injections were given twice a week.

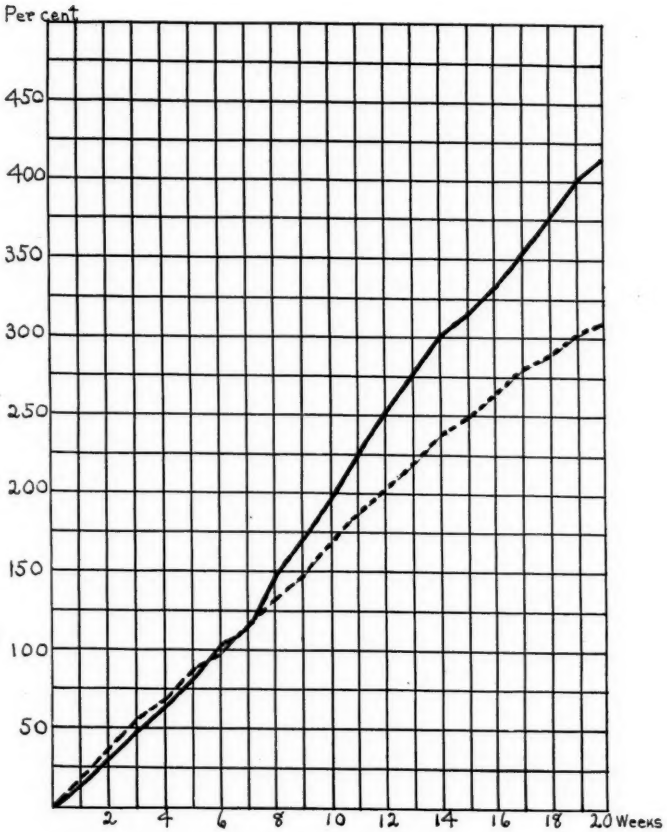
CHART 1



The initial dose for each thymus rabbit was two milligrams per one hundred grams of body weight. The dose was increased each week by one milligram per hundred grams to a maximum dose of ten milligrams per one hundred grams of body weight. This dose was continued to the end of the experiments. Each

control rabbit at the same time and under the same conditions received an injection of the glycerine-saline mixture proportion-

CHART 2

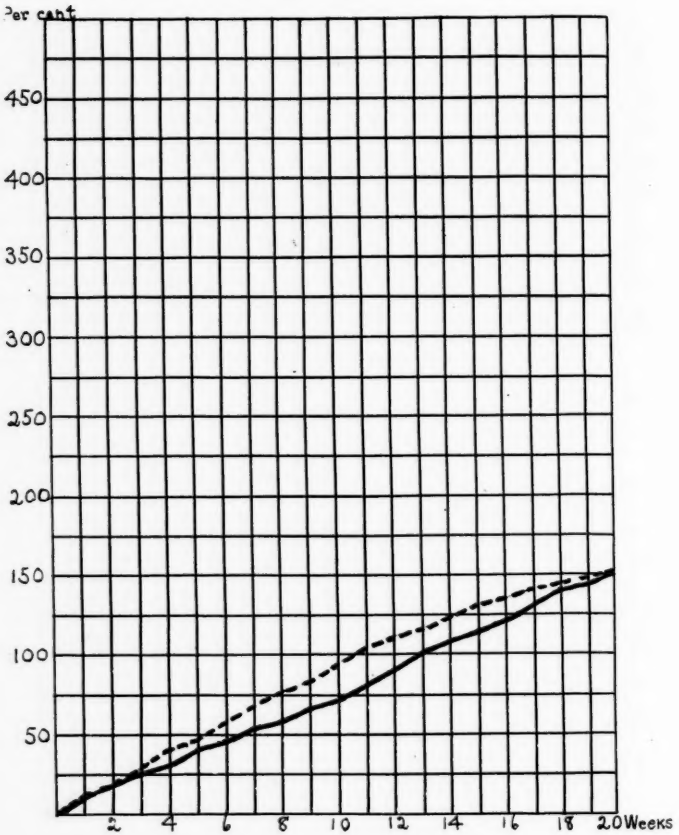


Percentage increase in growth of rabbits in group I
—— Control rabbits - - - - Thymus rabbits

ately equal in bulk. The injections were continued for twenty weeks, that is, until even the younger rabbits were apparently matured. One control and one thymus rabbit died during the course of the experiments. In both cases death occurred more than twenty-four hours after the last injection.

Each rabbit was weighed prior to injection. Growth and development progressed steadily in all. The average rate of

CHART 3



Percentage increase in growth of rabbits in group II
—— Control rabbits - - - Thymus rabbits

growth is shown in Charts 1, 2 and 3. For the first ten weeks the average percentage increase of weight in the thymus rabbits is slightly greater than in the controls; but during the second ten weeks the gain in weight is considerably greater in the controls.

At the end, the controls have gained 262.41 per cent, while the thymus rabbits have gained 215.38 per cent. When the animals are grouped according to age, as indicated in Table 1, and the average gain for each age group computed, a more striking difference is observed. From the eighth week on the control rabbits of Group I, the younger group, gained much more rapidly than the thymus rabbits until, at the end of the experiment, the former have gained 414.57 per cent as compared with 308.66 per cent for the latter. On the other hand, the older thymus rabbits, Group II, maintained to the end the slightly greater percentage gain shown by all the thymus rabbits in the early weeks. The younger rabbits presumably had more active thymus glands. It is possible that the thymus injections added to this higher degree of activity of the rabbit's own thymus may have been just sufficient to affect the weight as described.

TABLE 2
Control Rabbits

Number	Weight when killed	Reduced body weight R. B. W.	Weight of thyroid in mgm. per kilo. of R. B. W.	Weight of thymus in mgm. per kilo. of R. B. W.	Weight of spleen in mgm. per kilo. of R. B. W.
1	3.105	2.950	9.1	2383.0	647.7
7	3.055	2.613	63.9	540.7	213.5
10	3.260	3.078	61.0	1330.4	501.4
11	3.355	3.208	78.8	1049.8	499.6
15	1.630	1.485	121.8	1587.8	1740.7
18	2.200	2.012	95.9	1427.4	240.0
21	2.140	2.049	95.1	562.7	315.7
22	2.210	2.132	110.6	1386.0	253.7
Averages	2.619	2.440	79.5	1283.4	551.5

None of our rabbits developed muscular spasms or convulsions. Their behavior was normal so far as we could detect.

At the end of the twenty weeks the rabbits were killed and autopsies performed. The method employed was practically that of Livingston and as described in our previous report. The weight of the animal minus urine and contents of the gastrointestinal tract, i. e., reduced body weight, was determined. The thyroid and thymus glands and spleen were removed from each rabbit and weighed. The sexual apparatus was examined macroscopically. The reduced body weight and the weight of each of the glands removed, in milligrams per kilogram of reduced body weight, are given for the control rabbits in Table 2 and for the thymus rabbits in Table 3. A comparison of the figures shows that in the thymus rabbits the thyroid glands average 25.78 per cent heavier, the thymus glands 28.18 per cent lighter, and the

spleens 23.84 per cent heavier than in the control rabbits. A closer analysis reveals that the difference in the thyroids is confined to the younger group of rabbits. The average weight of the thyroids in the control rabbits of this group is 53.2 mgm. per kilogram of reduced body weight; the average weight of the thyroids in the thymus rabbits of the same group is 102.4 mgm. per kilogram of reduced body weight, a difference of 92.48 per cent. In the group of older rabbits, the thyroids in the controls averaged 105.8 mgm. and in the thymus rabbits, 96.8 mgm. per kilogram of reduced body weight, a slight difference in the opposite direction. We find the weight of the thymus reduced about equally in both groups. There is considerably more difference in the weight of the spleens of control and thymus rabbits in the

TABLE 3
Thymus Rabbits

Number	Weight when killed	Reduced body weight R. B. W.*	Weight of thyroid in mgm. per kilo. of R. B. W.	Weight of thymus in mgm. per kilo. of R. B. W.	Weight of spleen in mgm. per kilo. of R. B. W.
3	2.575	2.397	99.2	1236.1	878.1
5	2.360	2.154	109.0	1295.2	295.2
6	2.535	2.391	148.4	1082.3	506.0
8	2.475	2.222	100.3	1137.7	546.8
9	2.640	2.429	109.5	916.0	518.3
12	1.815	1.678	85.2	101.9	758.6
13	2.340	2.184	90.2	904.3	787.5
14	2.515	2.241	77.6	1599.7	708.1
16	1.990	1.905	75.0	570.6	640.4
17	1.685	1.579	155.1	1067.1	1732.1
19	2.175	2.032	78.7	211.1	499.5
20	2.310	2.102	66.1	973.8	568.5
23	2.185	2.017	94.1	842.3	554.2
24	2.315	2.200	112.2	966.8	579.5
Averages	2.279	2.109	100.0	921.7	683.7

younger than in the older group. In the former, the spleens of the thymus rabbits were 34.22 per cent heavier than those of the controls and in the latter, 19.57 per cent.

The most striking feature of these results is the increased weight of the thyroid glands of the thymus rabbits of the younger group. Burget has shown that high protein diets produce thyroid hyperplasia. It is possible that protein would have the same effect when injected hypodermically. The thymus preparation employed in these experiments obviously contained a large amount of protein. Therefore, we cannot say positively that the increased size of the thyroids is not due to protein. However, if the causative factor were protein, the change should have been just as marked in one group as in the other, since both received proportionately the same amounts of the preparation and, there-

fore, of protein. As we have pointed out, the difference was limited entirely to the group of younger animals.

The increased weight of the thyroids occurring in the same group of rabbits which showed the relative loss of body weight may be indicative of direct action of some active principle of the thymus. As already mentioned, its greater influence in the younger animals might be because the thymus glands of these younger rabbits were normally at a more active stage when the injections started.

The total weight of the thyroid gland in rabbit number 1 A, a female control, was only 27 mgm., 9.1 mgm. per kilogram of reduced body weight. The thymus gland in the same rabbit was larger than in any of the other rabbits. It weighed 7.030 grams or 2383 mgm. per kilogram of reduced body weight. This finding does not support the idea that hyperplasia of the thymus causes increase in the thyroid. The large thymus might of course have been compensatory to a deficient thyroid.

With two exceptions, the sex glands of all the rabbits appeared normal. There was only one testicle visible in number 15 E, a control, and at autopsy no sign of another could be found. The internal sexual apparatus of number 12 D, a female of the thymus group, was infantile in type. The thymus gland of this rabbit was extremely small. It weighed 101.9 mgm. per kilogram of reduced body weight, only a twelfth of the average weight of the thymus glands of the control rabbits. This defect of the sexual apparatus was congenital since the organs were not even at the stage of development to be expected in a rabbit of seven weeks, the age of this animal at the beginning of the experiments. While our thymus injections cannot be said to have caused the retarded development neither do they appear to have caused any improvement.

Eleven female rabbits were used in these experiments, of which six could have become pregnant, and four did become pregnant. Of the other two, one was a thymus rabbit, the other a control. One thymus and one control rabbit each gave birth to a normal litter during the twentieth week of the experiment. The other pregnancies were noted at autopsy (see Table 1). There is no evidence that the thymus injections exerted any influence upon the sex glands of these rabbits.

CONCLUSIONS

1. Subcutaneous injections of large doses of desiccated thymus substance, while checking the putting on of weight in young rabbits, did not otherwise impair growth or development.

2. A considerable increase in the weight of the thyroid gland and spleen and a decrease in the weight of the thymus were produced in young rabbits by subcutaneous thymus injections.

The expenses of this research were defrayed in part by a grant from the James Cooper Fund for Medical Research.

BIBLIOGRAPHY

Burget, G. E.: An attempt to produce experimental thyroid hyperplasia. Am. J. Physiol. (Balt.), 1917, **44**, 492.

Eddy, N. B.: The role of the thymus in exophtholmic goitre. Can. M. Assn. J. (Toronto), 1919, **9**, 203-212.

Livingston, A. E.: Effect of castration on the weight of the pituitary and other glands of internal secretion in the rabbit. Am. J. Physiol. (Balt.), 1916, **40**, 161.

Olkon, D. M.: The effect of thymus gland injection on the growth and behavior of the guinea-pig. Arch. Int. Med. (Chgo.), 1918, **22**, 815.

PRACTICAL ORGANOTHERAPY. The Internal Secretions in General Practice. By Dr. Henry R. Harrower, Glendale, Cal. The Harrower Laboratory, 1920, 268 p.

This is an ambitious little book written by an optimistic endocrinologist who attempts to crowd into 268 pages a resume of all the present knowledge on endocrinology and organotherapy. He succeeds in presenting his views on the subject in a readable and interesting manner, but with no great success as to scientific accuracy. The book contains statements which have not as yet been accepted, advancing claims which some experimenters and clinicians would be slow to accept.

All in all, this book must be considered in the light of a commercial publication and accepted in the same class as, for example, Merck's Index. Considering it from that viewpoint, the general practitioner will find many helpful hints on an interesting and timely subject.—M. B. G.

QUATRE LECONS SUR LES SÉCRÉTIONS INTERNES. By Prof. Eugene Gley, Paris. Paris, 1920, Baillière et fis, 154 p.

Professor Gley is competent, as few are, to indicate the course of development of endocrine science and to discuss the philosophic aspects of the subject. In a series of four lectures delivered before the "Sociedad de Biologia" of Barcelona in 1917, an engaging presentation of the matter was made, and the lectures are now fortunately available in book form. The topics covered were: the evolution and present status of the endocrine question; the physiological conditions necessary to internal secretion; new orientation of researches upon hormones and hormazones and, finally, the essential results of the study of the internal secretions—a revolution in biology.

The first chapter is a critique on the general doctrine of the internal secretions, centering about the work of Claude Bernard. As to the present status of endocrinology, Gley reminds us again that the doctrine has not acquired precision and stability *pari passu* with the rich accumulation of new facts. The field is encumbered with incomplete experiments, adventurous hypotheses, vain theories and even errors. Experimental observations are often applied without reflection and, indeed, without logic,—both of which, one may add, are eminently required.

In the second chapter are defined the precise conditions that must be met before an endocrine function can be postulated. Sundry new "Hormones" have been introduced which

we might have been mercifully spared had their sponsors comprehended these principles. To any who are sanguine of finding "hormone x" or y or z, this chapter is especially commended.

The third chapter comprises a critical discussion of methodology and the fourth, a formulation of a conception of the significance of endocrinology in the field of general biology.

In the present stage of development of our subject, all sorts of attempts at exposition of its underlying philosophy are perhaps to be expected. It is fortunate when, as in this case, the expositor is a master in the field, who has gone both deep and wide.—R. G. H.

ABSTRACTS

ACHONDROPLASIA, Effect of—on menstruation. Miller (J. L.), West Va. M. J. (Huntington), 1920, **14**, 366-367.

The article gives a brief resume of the leading characteristics of achondroplasia, and a report of two cases that have been under observation for twenty years, particularly in regard to their menstrual life.

The characteristics common to both patients were: both had mothers under the normal female stature, but normal in every other way; both were members of large families, their brothers and sisters being normal, except in one case they were slightly under normal adult stature. No history of other dwarfs in either family, and no evidence or history of thyroid trouble in either patient or any member of their respective families was elicited.

One patient, aged 26 years, height 4 feet 2 inches, weight 126 pounds, physical development typically achondroplastic, intellect excellent, began menstruating at the age of two weeks, the lochia having the gross appearance of an adult female, and has continued at twenty-eight day intervals until December, 1918, when she went into the menopause with the characteristic nervous and physical phenomena of this condition in the normal female. Pubic hair appeared at age of five or six years and breasts and facial appearance became that of the mature adult.

Case two: the subject was twenty-five years old, 3 feet 11 inches in height, and 125 pounds in weight; all features were very typical of achondroplasia, especially the marked bowing of the femurs and bones of both legs. The intellect was normal. Pubic hair and development of the breasts appeared about the 12th to 15th years, but no indication of the menstrual flow appeared until the twenty-first year, though for several months preceding the appearance of the flow there was a general malaise for a few days at four to six weeks' intervals. Corpus luteum and thyroid extract were tried at different times in the second case, but with no apparent result.

The conclusions are that the menstrual phenomena in these cases, and probably the physical development as well, were

due to some severe disorder of the endocrin system, and that probably in the first case certain hormones which normally stimulate growth and development of the sexual functions were present to an excessive degree, and in the second case insufficient or nearly suppressed.—Author's Abst.

ADIPOSIS DOLOROSA (Zur Kenntnis der Adipositas dolorosa). Grafe (E.), München. med. Wchnschr. 1920, **67,** 339-341.

The author describes a case in a woman of 21. The disease began at the same time as the beginning of menstruation, with psychical alterations, and gradually increasing adiposity. The blood sugar was normal. The thyroid could not be palpated. The symptoms are not those of Dercum's disease, for in Dercum's disease pain is not spontaneous, but the tumors are painful only upon pressure; such condition did not obtain in this case. There was a certain degree of periodicity in the symptoms. The patient showed an enormous retention of water. Oophorin, hypophysis and thyroidin had a good influence, as well on the retention of water as on metabolism, but were not able to cure the disease.—J. K.

ADIPOSITY, Cerebral versus lacteal—. Reuben (M. S.), Arch. Pediat. (N. Y.), 1919, **36,** 636.

To prove that every fat baby has not a tumor of the pituitary, the author reports a case of a girl, 10 months of age, who gave the following dimensions: circumference of head, 17½ inches; chest, 24¾ inches; length, 29½ inches; mid-thigh, 15¾ inches; mid-leg, 10½ inches. The anterior fontanel was closed. She did not show any symptoms of dyspituitarism; there was no hyperglycemia, no reaction to pituitary extract. The Wassermann was negative. The eye grounds were normal. An analysis of the mother's milk showed 6 to 7 percent fat, which the author felt accounts for the adiposity. He also reported another case of a child who weighed 7 pounds at 7 months and 35 pounds at one year of age. When last seen at the age of 6 years, she had not shown any signs of hypopituitarism.

—M. B. G.

(ADRENALS) Addisonian symptom complex. (Addisonscher Symptomenkomplex.) Wien. klin. Wchnschr. (Vienna), 1918, **31,** 799.

A classical case. No new data.—F. S. H.

(ADRENALS) The time relations of the blood pressure changes after excision of the adrenal glands, with some observations on blood volume changes. Bazett (H. C.), J. Physiol. (Lond.), 1920, **53,** 320-339.

The experiments described consist of some controls made at the commencement of an investigation of the relation of the adrenals to vascular tone. Animals may survive one to three days after excision of the adrenals, but low blood pressure is found some time previous to death. The time of development of these changes has not been carefully investigated.

Most of the work was done on cats; a few experiments were also made on rabbits. The rate of the fall of blood pressure was measured in animals in which the glands were removed under ether and which were then allowed to recover; in animals under continuous urethane anesthesia, and in animals previously decerebrated. It was found that excision of the adrenals in the cat is not followed immediately by a fall of blood pressure, but the changes develop more rapidly in decerebrate animals than in those under urethane anesthesia. They are least rapid in ether anesthesia followed by recovery from the ether. Urethane anesthesia may be used in cats for experiments lasting twenty-five hours or longer. The pressure falls 10 to 20 per cent lower than in ether or decerebration, and after eight hours of anesthesia may fall still further. Decerebrate preparations may be used for blood pressure experiments lasting several days, if care is used. Excision of the adrenals in a urethanized cat causes a fall in blood pressure in two or three hours, and death results in about ten and one-half hours. In the decerebrate cat excision of the adrenals is followed by a fall of pressure in one hour, and death in six hours. In ether anesthesia it is eighteen hours before the fall reaches 30 to 40 per cent. With excision of the adrenals there is an immediate slight dilution of the blood, but later as the pressure falls there is little further dilution. After adrenal excision under urethane, the various types of response to sciatic stimulation could not be obtained with any degree of constancy.—T. C. B.

ADRENAL insufficiency, Anatomical clinical study of two cases of—(Étude anatomo-clinique de deux cas d'insuffisance surrénale). Betchov (N.) and Demole (V.), Rev. méd. de la Suisse Rom. (Geneva), 1918, **38,** 379-386.

A detailed description of two cases of adrenal insufficiency presenting nothing new but substantiating the idea that "Ser-

gent's line'' is clinical evidence of a lessened adrenal efficiency. —F. S. H.

(ADRENALS) Addison's disease (Maladie bronzee d'Addison). Boinet, Marseilles med., 1918, **55,** 176-181.

A clinical report and autopsy findings of two cases of Addisonian coma following extreme fatigue. In three non-fatal cases adrenal opotherapy was successful in ameliorating the distress.—F. S. H.

(ADRENALS) A case of Addison's disease. Cabot (R. C.), Case Records Mass. Gen. Hosp. (Bost.), **6,** 920, No. 18, part 1.

The case of a carpenter aged sixty-four years is presented. The patient's family history is negative and his health had been unusually good. At twenty-four he had measles; at thirty-two typhoid fever without sequelae, except constipation. For ten years he had hemorrhoids with a little bleeding. He had occasional headaches. Before the typhoid fever he weighed 230 pounds, his best weight. His usual weight has been 190, and he thinks he has lost about fifty pounds in the past two years.

The patient's bowels have been irregular and constipated, especially for the past three or four years. Three years ago for a period of two weeks he was nauseated, and regurgitated all food in a few minutes after it had been taken. He was in bed on a diet. He recovered and again ate the same kind of food as the rest of the family, but less of it. He went back to his work. One year later he had a similar but much less severe attack lasting for a week. For five months he missed one or two days' work in a month, and then two months ago he gave up work entirely on account of general weakness. Since then, also, he has been unable to retain anything but a quart of milk a day, malted milk, spinach, and an occasional cracker. There has been no pain.

Examination revealed that there was no expansion of the left lung during respiration and the x-ray plate gave the appearance of an old tuberculous infection involving both lungs and the left pleura. Pulse, 92 to 129, was of poor volume and tension. Blood pressure: systolic 110, diastolic 80. Urine and stools negative. Blood: hemoglogin 70%, leucocytes 12,880 with 57% polynuclears, slight anisocytosis; Wassermann reaction negative.

The patient died on the third day after admission and autopsy revealed: tuberculosis of the adrenals by which they

were transformed into fibrocalcarous masses; arteriosclerosis and dilatation of the heart; chronic pleuritis; absolute tuberculosis of the bronchial lymph nodes, and cholelithiasis.—J. F.

(ADRENAL) The pathology of experimental rabies. I. The kidneys, adrenals, liver and spleen. Cornwall (J. W.), Indian J. Med. Research (Calcutta), 1919, **7**, 148-159; Abst., Chem. Abst., 1920, **14**, 2204.

Hyperglycemia is a late phenomenon in fixed-virus rabies. It is sometimes followed by glycosuria. There is little change in the glycogen content of the liver. The urine becomes acid (rabbits) and globulins are excreted with but little albumin. The specific gravity of the urine falls markedly on the 5th day and the percentage of chlorides at first increases and then decreases. The weight of the adrenal gland increases by one-third and autolytic changes occur, chiefly in the medullary cells. Kymographic studies show a diminution in the pressor effects of adrenal gland extracts during the 48 hours following sub-dural inoculation. This is followed by recovery and then toward the end of the disease there is a second diminution in the quantity of pressor substances. Chemical tests show a diminution of adrenaline in the adrenal glands of rabbits succumbing to fixed-virus rabies and also of guinea-pigs dying from intramuscular inoculation with street virus. It is concluded that growth of the rabies organism in the central nervous system causes irritative stimuli to pass along the splanchnic nerves to the adrenals and liver and gives rise to the discharge into the blood stream of an excess of sugar. Sometimes an excessive secretion of adrenaline occurs. Much damage is caused to the kidneys and adrenals by toxic agents in the blood derived from the growth of the rabies organism in the central nervous system.—R. G. H.

(ADRENAL) The pharmaco-dynamics of quinine. II. Some effects of quinine on the adrenals, kidneys, and spleen of healthy rabbits. Cornwall (J. W.), Indian J. Med. Research (Calcutta), 1919, **7**, 160-166.

Quinine administered intravenously and intramuscularly to rabbits over a period of 9 months causes damage to the cellular elements of the adrenals and kidneys and increases the rate of disintegration of the red blood corpuscles in the spleen.—Chem. Abst., **14**, 2218.

(ADRENALS) Direct transmission of Addison's disease (Transmission directe de la enfermedad de Addison). Es-

pina, Real Acad. Nac. de Medicina (Madrid), 1919, ——, —— (Mch. 15).

Espina gives a clinical description of two boys with Addison's disease whose father had died of the same disorder. The opinion is expressed that these cases arose through direct transmission from the father to the sons.—E. B.

(ADRENALS) Some observations on the functions of the suprarenal glands, in white rats. Exner (H. V.), Dublin J. Med. Sc., 1920, **4,** 79-89.

Investigation by means of asphyxiation experiments, performed on white rats, showed, that despite the presence of the adrenals, a fall of blood pressure was noted, similar to that in animals from which the adrenals were removed. This investigator concludes, therefore, that the adrenals normally play no part in the rise of blood pressure, despite the fact that an injection of adrenal extract produces this phenomenon. He also found that when the central end of the vagus was stimulated in those animals from which the adrenals were extirpated, sugar was found in the urine. He concludes that "the glycogenic function of the suprarenals is dependent on, or works in conjunction with, some nervous control, which functionates, at least in part, even in the absence of these organs."

—J. H. L.

(ADRENALS) Symptoms produced by the plexus solaris in tuberculosis of the lungs (La sindrome solare negli ammalati di tuberculosi polmonare). Gallotti (A.), Il Morgagni (Milano and Napoli), 1920, **62,** 81-96.

The author observed in two cases of tuberculosis of the lungs symptoms resembling tabetic crises or lead colic. No changes in the abdomen could be detected, even at autopsy. The "ligne blanche surrénale" of Sergent was present, and there was low blood pressure. Defective functioning of the plexus solaris is probably the cause of these symptoms. This point the author discusses in some detail. Cases have been described in which the plexus was compressed by tuberculous tissue; but even without these gross changes the affinity of the sympathicus for the toxins of the tubercle-bacillus is well known. The primary affection here is probably insufficiency of the sympathicus, the secondary, insufficiency of the adrenals.

—J. K.

(ADRENALS) The significance of the chromaffin system (Die Bedeutung des chromaffinen Systems). Hart (C.), Ztschr. f. ärztliche Fortbildung (Jena), 1920, **17**, 221-225.

An interesting general discussion without new facts. The author believes that Addison's disease is caused by a pathological process in the adrenals in patients with a hypoplastic constitution. As Graves' disease is also found in persons with this constitution the (very rare) combination of Graves' and Addison's diseases may perhaps be explained on the same basis. —J. K.

(ADRENAL) A case of uterine epithelioma presenting the typical characteristics of cortical suprarenaloma (Un cas d' epithéliome utérin presentant les caractères typiques du cortico-surrénalome). Hartmann (H.) & Peyron (A.), Gynec. et Obst. Rev. Mens. (Paris), 1920, **1**, 1-19.

The review of the literature reveals 11 reported cases of tumors of suprarenal type occurring in the internal genital organs of women. The paper is a report of a case operated upon by the authors. It was found that the broad ligaments were free and the tumor was intrauterine. Nine plates are shown of the histological findings compared with normal material.—F. S. H.

ADRENAL insufficiency in the infections (Insufficiencia suprerenal en las infecciones). Marañón (G.), Acad. med.-quir., 1919, ——, ——, (Mch. 18).

In all infectious diseases there are frequently accidents of the nature of collapses which have been heretofore attributed to alterations of the myocardium, the question of suprarenal insufficiency should be considered. Both types occur. These glands possess two functions, the one an antitoxic, protective function accomplished by the internal secretion of cholesterol of cortical origin, and the other the tonic effect of adrenalin of medullary origin. When this latter is diminished or lacking, collapse is produced. These accidents can be either chronic or acute; the first recall cases of Addison's syndrome; the second are rapid syncopes with hypothermia and asthenia resembling shock. They are very frequent in diphtheria and typhoid; sometimes they are observed in exanthematous typhus. Autopsy often shows small suprarenals with little adrenaline and cholesterol. During the life of the patient these constituents are seen to diminish in the blood. From these facts it follows that adrenaline should be administered in the form of extracts

of the whole gland in those infections in which collapse is feared.—E. B.

(ADRENAL) Nicotine apnea. Ozorio de Almeida (A.), J. de physiol. et path. gén. (Par.), 1920, **18,** 744-752.

When nicotine is injected intravenously into anesthetized dogs, a prolonged arrest of respiration is produced which can properly be called nicotine apnea. It is not due to the sharp rise in blood pressure following the injection since double vagus section does not inhibit the apneic effect. Neither stimulation of the central end of the cut vagus, nor ablation of the adrenals prevented the appearance of the characteristic reresponse.—F. S. H., Chem. Abst., **14,** 2219.

ADRENALS, Chloroform narcosis and the— (Chloranarcozi e funzioni surrenale). Pitini (A.), Gazetta degli Ospedali (Milano), 1920, **41,** 415.

After narcosis with chloroform the content of adrenalin in the adrenal glands is diminished. Perhaps the high blood pressure in the beginning of narcosis and the low pressure during the rest of this period may be explained in this way, that first the chromaffine system is stimulated and produces more adrenalin. This would be followed by an exhaustion of the chromaffine system. [This idea was proposed by Elliott years ago.] The suggestion is again offered that injections of adrenalin are of use in narcosis.—J. K.

(ADRENAL) A case of hypernephroma in the renal hilus. Stenström (N.), Hygiea (Stockholm), 1919, **81,** 843-851.

The tumor, which occurred in a woman of 46 years, was the size of a Mandarin orange. It was histologically benign. —J. A. H.

(ADRENALS) Further observations on the relation of the adrenals to certain experimental hyperglycemias (ether and asphyxia). Stewart (G. N.) & Rogoff (J. M.), Am. J. Physiol. (Balt.), 1920, **51,** 366-377.

The paper is an answer to recent critics, especially Kellaway, with some new experiments to show that epinephrin output is not essentially concerned in the hyperglycemia induced by ether narcosis and by asphyxia.—T. C. B.

ADRENAL bleeding in the new-born (Ueber Nebennierentblutungen bei Neugeborenen). Toepffer (H.), Arch. f. Gynaek. (Berlin), 1920, **112,** 342-356.

A clinical and post-mortem description of an infant dying three days after birth with some evidence of adrenal involvement. The histological picture of the adrenals seems to justify the conclusion that the condition is the result of a primary, early occurring fatal thrombosis of the suprarenal vein, which in turn has caused chronic fibrous induration and local parenchymal necrosis. There had taken place extravasation of blood into the necrotic area. As a consequence of the act of birth arterial congestion apparently had occurred, resulting in a still further escape of blood into the tissues.—F. S. H.

(ADRENAL) The action of adrenin and of various extracts of glandular organs on veins. Tugane (S. H.), Sei-I-Kwai M. J. (Tokyo), 1919, **38,** 51.

Cow's method, with but slight alterations, was employed for registering the contractions of the veins which were obtained from freshly killed pigs, dogs and cats. The author observed that ring preparations of veins, when treated with adrenin, contract with reduction in volume just as do arteries, which indicates, in his opinion, that they are probably supplied with sympathetic venoconstrictor fibers. He found, on the other hand, that treatment with saline extracts of lymph gland, spleen, kidney, liver and muscles brings about a dilation of the ring preparations, indicating perhaps the existence of venodilator fibers. No histological evidence is presented.

—E. V. C.

ADRENAL syndrome, Contribution to the study of— (Contribution al estudio de los sindromas suprarrenales). Venegas (F.), La Clin. Castellana. 1919, ——, ——.

General review.—E. B.

ADRENIN, The intravenous injection of—in the treatment of hemorrhage (A propos des injections intraveineuses d'adrénaline dans le traitement des hémorragies). Bardier (E.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 91-94.

A continuation of studies already reported (see Endocrin. **4,** 105). Two experiments on exsanguinated dogs showed that in spite of the loss of blood and the serious symptoms resulting, the intravenous injection of adrenalin causes hyperten-

sion, acceleration and augmentation of the heart beat, and resumption of respiration. The action is of short duration—three to four minutes—but can be reproduced by successive injections.

Two observations on human subjects are also reported: one was a man of sixty with a severe crushing of the lower extremities and loss of blood, the other a woman, exsanguinated by rupture of a fallopian tube. Both cases responded to the adrenalin, but only the woman recovered. She lived eight days, and then died of pneumonia. The proceeding seems indicated as an extreme emergency measure, and may keep the heart going while preparations are made for transfusion.—T. C. B.

ADRENALIN, The effect of the subcutaneous injection of—on the heat production, blood pressure and pulse rate in man. Boothby (W. M.) & Sandiford (Irene), Abst., Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51**, 200-201; in full, Ibid, 407-421.

The results are reported of forty-six experiments on groups of patients showing variations in the activity of the thyroid, pituitary or adrenals, as well as a small group of normal controls. Adrenalin causes an increase in heat production, increase in the respiratory quotient, ventilation rate, respiration rate, heart beat per minute, volume of each beat, peripheral vascular dilatation and systolic and diastolic pressures. Not all come into play in any one case, but some combination. There is no relationship between the character of the adrenalin reaction and the degree of activity of the thyroid, and therefore the reaction is not indicative of the presence or absence of hyperthyroidism. The metabolic rate curve is similar to that of carbohydrate plethora and suggests the possibility that the increased heat production may be due to an excess of carbohydrate metabolites. There may also be direct chemical stimulation of cellular combustion.—T. C. B.

ADRENALIN treatment of rachitis (La adrenalina en la tratamiento del raquitismo). Corominas (F.), Arch. Españ. de Pediat. (Madrid), 1919, **3**, 215-224.

The author reviews the current theories with respect to the etiology of rachitis and insists that every case is accompanied by an endocrine dysfunction, which paves the way for the alimentary toxemias, etc. The parathyroids, thymus and suprarenals are the glands which play the major role in this

process by reason of their influence on the calcium metabolism. Corominas has used several extracts of endocrine glands as therapeutic agents and considers that adrenaline produces the best results, since it acts directly and at the same time whips up the endocrine system as a whole. It is preferably administered by the gastric route two to three drops daily of the one to a thousand solution.—E. B.

ADRENALIN, The excretion of—according to recent studies, particularly of G. N. Stewart and his students (De l'excrétion de l'adrénaline d'après les travaux récentes, particulierment cieux de G. N. Stewart et de ses élèves). Heitz (J.), Arch. de. mal du coeur (Paris), 1918, **11**, 215-218.

A review.—F. S. H.

Concerning ADRENIN. I. The alterations of the vasopressor action of adrenalin after its treatment with bacterial products (Zur Kenntniss des Adrenalins. I. Über die Änderung der blutdrucksteigeinden Wirkung des Adrenalins nach Behandlung desselben mit bakteriellen Produkten). v. Gröer (F.) & Hecht (A. F.); Biochem. Ztschr. (Berlin), 1920, **102**, 1-12.

When adrenalin is kept in contact with diphtheria toxin for a considerable period of time it loses its ability to cause an increased blood pressure in dogs. The bacterial nucleo-proteins have a still greater destructive action. This disturbing effect cannot be attributed to the presence of free OH-ions. When the toxin or the bouillon is boiled they are much less, if at all, active in destroying the effectiveness of adrenalin.—F. S. H.

Concerning ADRENIN. II. The alterations of the vasoconstrictor action of adrenalin under the influence of different hydrogenion concentrations and after its treatment with bacterial products and proteins (Zur Kenntniss des Adrenalins. II. Über die Änderung der gefässverengenden Wirkung des Adrenalins unter dem Einfluss verschiedener Wasserstaffionenkonzentationen und nach Behandlung desselben mit verschiedenen bakteriellen Produkten und Eiweisskörpern). v. Gröer (F.) & Matula (J.), Biochem. Ztschr. (Berlin), 1920, **102**, 12-38.

Under anerobic conditions alkali reacts on adrenalin to cause an initial increase followed by a decrease of its vasoconstrictor activity. This is accomplished through retarding the oxidation of adrenalin, the optimum effect being obtained

between PH=7.5 and PH=8.5. Contact with bacterial nucleoproteins has a similar effect even under anerobic conditions and regardless of the reaction of the medium. This property of the nucleoproteins is weakened by heating. Both nucleoproteins and other protein compounds retard the oxidation of adrenalin through which an air-current is passed: this reaction occurs regardless of the reaction of the medium and is lessened if the proteins be heated. Many true proteins, and also tuberculin, cause an increase in the adrenalin activity after long contact under anerobic and H atmospheric conditions; while they exert an inhibitory action on the disturbing effect of OH-ions. The adrenalin disturbing action of the diphtheria toxin is complex and bound up with the nucleoprotein as well as with the OH-ion activity.—F. S. H.

(ADRENIN) Bodily symptoms caused by emotion (Lichamelijke afroijkingen tengevolge van emotie). Kooy (F. H.), Neder. Maandschr. Geneesk. (Leiden), 1920, **1**, 29-44.

Cannon has reported that emotion (fear, rage) causes hyperactivity of the sympathicus and a hypersecretion of adrenalin. The author found in agitated patients with psychoses a higher amount of blood sugar and a higher blood pressure than normal. It is suggested that the changes in temperature (hysterical fever) and in the function of the intestines during emotion may perhaps be explained in the same way.—J. K.

ADRENIN, Action of Röntgen rays on—. Lüdin (M.), Strahlentherapie, 1918, **8**, 441; Zentralbl. f. Biochem., u. Biophys., **21**, 179.

Previous observations of Richter and Gerhartz have indicated that the action of adrenaline is impaired or inhibited by Röntgen rays. L. was unable to confirm these observations. By determining adrenaline according to the Magnus procedure in the surviving intestine, L. found that no change in the activity of adrenaline on account of the action of Röntgen rays could be detected.—Chem. Abst. **14**, 1125.

(ADRENIN) The substance in the blood-serum resembling adrenalin (Over de op adrenaline gelikjende stoffen in bloedserum). Rassers (J. R. F.), Nederl. Tijdschr. v Geneesk. (Haarlem), 1920, **64**, 785-791.

Of no immediate endocrine interest.—J. K.

(ADRENIN) The practical value of curved needle injection in the intercricothyroid region (La pratique usuelle de l' injection intercricothyroidienne par l'aiguille cousle). Rosenthal (G.), Bull. gén. therap. (Paris), 1920, **171,** 156-158.

Of technical interest, and mention of the use of adrenalin by this method.—F. S. H.

Effects of ADRENIN (Adrehalinwirkungen). Schlesinger (H.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 335.

A short note to the effect that injections of adrenalin in the aged may cause stenocardia and a fall of blood pressure. This may be explained by the fact that adrenin has an effect on the vasoconstrictor as well as on the vasodilator mechanism.—J. K.

(ADRENIN) Vascular reaction to epinephrin in perfusates of various H-ion concentrations. Snyder (C. D.) and Campbell (W. A., Jr.), Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51,** 199-200.

Confirmatory evidence is given to show that the reversal (dilator) effect of epinephrin may be due to H-ion concentration.—T. C. B.

(ADRENIN) Further observations on the relations of the central nervous system to epinephrin secretion. Stewart (G. N.) & Rogoff (J. M.), Abst. Proceedings Am. Physiol. Soc., Am. Jour. Physiol. (Balt.), 1920, **51,** 175-176; in full, Ibid, 484-524.

Former experiments on the epinephrin output after transection of the spinal cord at different levels in cats have been confirmed and extended by a new series of experiments. After section of the cervical cord the output of epinephrin was undiminished in several animals, while in others it was more or less diminished. When the brain and bulb were eliminated there was a full normal output. In survival experiments the output was one-half to one-third the normal average. In acute experiments with dorsal cord transections, the output was greatly diminished or abolished. Strychnine caused a marked increase in the output in both acute and survival cases. Further experiments on cats with denervated hearts confirm their previous conclusion that the reactions obtained do not constitute a demonstration of epinephrin output with asphyxia and nerve stimulation (as reported by Cannon and von Anrep), until it is

sh own that redistribution of the blood with normal output cannot account for the reactions.—T. C. B.

(ADRENIN) Case of ptyalism during pregnancy treated with adrenalin (Un cas de ptyalism gravidique traité par l'adrénaline). Trillat (P.), Bull. Soc. Obst. et Gyn. (Paris), 1919, **4**, 85-87.

A primipara of 30 years complained of excessive salivation. On examination it was found that the patient was secreting from 900 to 1100 cc. of saliva daily. The daily oral administration of 10 drops of adrenalin 1:1000 for 3 weeks resulted in a gradual diminution of the output to normal.—F. S. H.

ADRENALINE, The use of—in obstetrics (Empleo de la adrenalina en la obstetricia). Udaeta, Soc. Ginecol. Española, 1918, ——, —— (Feb. 6).

This paper presents the clinical case histories of two cases of suprarenal insufficiency during pregnancy showing asthenia, hypotension, lumbar-abdominal pains, vomiting and Sergent's line. The administration of thirty drops of adrenaline a day generally resulted in relief of the symptoms and the satisfactory completion of the pregnancy at term.—E. B.

ADRENIN, Treatment of gestation osteomalacia with— (Behandlung des Gestationsosteomalazie mit Adrenalin). Wagner (G. A.), Wien. klin. Wchnschr. (Vienna), 1920, **33**, 324; Deutsche med. Wchnschr. (Berl.), 1920, **46**, 423.

Data reported elsewhere. See Endocrin., **4**, 247.—J. K.

ADRENIN, Treatment of influenza with— (Grippebehandlung mit Adrenalin). Wagner (G. A.), Wien. klin. Wchnschr. (Vienna), 1920, **33**, 324; Deutsche med. Wchnschr. (Berl.), 1920, **46**, 423.

Data reported elsewhere. See Endocrin., **4**, 247.—J. K.

ADRENIN, Abdominal complaints cured by— (Buikklachten onderdrukt door adrenaline). van Waveren (A. G. W.), Med. Tijdschr. v. Geneesk. (Haarlem), 1920, **64**, (i), 1716-1717.

From a patient with abdonimal pains the appendix was removed. During the operation pericolitis was observed. The operation had no influence on the pain, but it disappeared when 25 milligrams a day of dried adrenal gland was given.

The pain returned as soon as the administration of the adrenal was discontinued.—J. K.

(AUTONOMIC N. SYST.) Constitutional kinesthopathy (I cenestopatici constituzionali). Buscaino (V. M.), Riv. di Patol. nerv. e ment. (Firenze), 1918, **23,** 257-285.

The author during the war was struck by the unusual number of cases coming under his notice with such ominous diagnoses as epilepsy, dementia precox, etc., who after a time completely recovered. From the total number he was able to differentiate a group of two hundred with sufficient similarity as to permit their classification as "Constitutional cenestopathics." These are discussed in detail. Their general characteristics were neuropsychopathic heredity, cranial and facial asymmetry, abnormal kinesthesia, great irascibility and marked irritability throughout the vegetative mechanisms. They were predominantly sympathicotonic, as shown, for example, by tachycardia and vasomotor instability. For numerous other details those interested should consult the original.
—G. V.

CORPUS LUTEUM, The physiology of the—. Hermann (E. T.), Minnesota Med. (St. Paul), 1918, **1,** 181-185.

A general discussion containing no new data.—F. S. H.

CORPUS LUTEUM extract, The use of—hypodermically in cases of repeated abortion without demonstrable cause. Hirst (J. C.), Am. J. Obst. (N. Y.), 1918, **77,** 662-664.

A report of three patients with histories of repeated abortion, two of whom were enabled to carry to term and deliver infants by the empirical use of 1 cc. of corpus luteum extract administered hypodermically once daily for periods of nine weeks. The cases were discussed and the results favorably commented upon.—F. S. H.

(CORPUS LUTEUM) The question of ectopic decidua (Zur Frage der ektopischen Deszidua). Lahm (W.), Arch. f. Gynaek. (Berlin), 1920, **112,** 427-435.

A description of the histological pictures of the decidua of a case of ectopic pregnancy, in which it is shown that no structural differences exist between this type and that found in the uterine decidua of two months or over. Since the case showed no histo-pathological structures L. is inclined to be-

lieve that the phenomenon is attributable to an abnormality in the locus of action of the corpus luteum secretion giving the decidual reaction.—F. S. H.

(CORPUS LUTEUM) The origin of the corpora lutea. Westman (Ax.), Hygiea (Stockholm), 1919, **81,** 865-879.

The author considers that the lutein cells originate from the cells of the vascular epithelium.—J. A. H.

DIABETES, Experimental studies on—. Series 1. Production and control of diabetes in the dog. Gross anatomic relations of the pancreas. 2. Effects of carbohydrate diets. Allen (F. M.), J. Exper. M. (Balt.), 1920, **31,** 363-380. Ibid, 381-402.

These studies were based upon a form of diabetes produced by the removal of the greater part of the pancreas of animals, leaving a remnant about the duct secreting normally into the duodenum.

Allen reports an extensive series of studies upon dogs in which, by removal of the greater part of the pancreatic tissue, a diabetes closely similar to the clinical human type is produced. It was found that the injurious effects of excessive carbohydrate diet are demonstrable in partially depancreatized dogs, in the same manner as in human patients. With severe diabetes there is rapid progress of emaciation and weakness and early death. With milder diabetes, there is frequently a transitional state following operation, when the fate depends on the diet. If the tolerance is spared for a time, recovery sometimes occurs to such extent that diabetes cannot be produced by any kind or quantity of feeding, but only by removal of a small additional fragment of pancreatic tissue. The proper degree of carbohydrate overfeeding is important in this early period for producing the most useful type of diabetic animals; namely, those having good digestion and general health combined with a permanent lowering of assimilative power, like the condition of human patients. In the early stage, glucose is more powerful than starch in producing diabetes, and animals which are progressing toward complete recovery on starch diet can be sent into hopeless diabetes by admixture of glucose. The difference seems to be merely of the rate of absorption, and indicates that a rapid flood of carbohydrate is more injurious to the pancreatic function than a slow absorption. Whenever permanent diabetes is present, so that complete recovery is impossible, starch brings on glycosuria more slowly than sugar, but just as surely. The difference in time in different cases amounts to days, weeks, or

months. The clinical lesson from such experiments is that even if a patient becomes free from glycosuria on withdrawal of sugar only, nevertheless other foods should also be limited. No significant differences were observed between the assimilation of different starches, or any extreme lowering of the carbohydrate tolerance by proteins, such as alleged by certain writers in connection with the "oatmeal cure." Repair of traumatic inflammation and hypertrophy of the pancreas remnant have been mentioned incidentally as the basis of the early tendency to recovery, and also hydropic degeneration of Langerhans islands as an accompaniment of the lowering of tolerance by excessive diet. These are believed to have their parallels in human cases, and are to be described more fully hereafter.—B. T. S.

DIABETES, Acidosis in relation to—. Anklesaria (B. N.), Indian M. Gaz. (Calcutta), 1919, **54,** 96-98.

A didactic exposition of the author's opinion that diabetes is caused by a low type of latent toxemia affecting the internal secretion of the pancreas.

DIABETES mellitus and war diet in Vienna (Diabetes mellitus and Kriegskost in Wien). Elias (H.) and Singer (R.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 561-562.

In Vienna, as well as in Berlin, the underfeeding incident to the war has had a good influence on diabetes. There are, however, differences. In Berlin the patients showed glycemia even when the urine was sugar-free; in Vienna, when there was no glycosuria the amount of blood sugar was lower than normal. In Vienna, elderly patients with diabetes during the war were in better condition than young patients. The good influences of underfeeding most probably are to be attributed to the small quantities of proteins ingested.—J. K.

DIABETES, The significance of extreme hyperglycemia in— (Zur Frage der Bedeutung extremer Hyperglykämie beim Diabetes mellitus). Friedländer (G.) Berlin. klin. Wchnschr., 1920, **57,** 207.

A man of 22 years showed diabetic symptoms for 3 weeks and died in coma. This coma was not the sort characteristic of diabetes, for there was no acidosis or air hunger. The urine contained 6 per cent of sugar and the blood, 1.03 per cent. The author considers this as a case of death by intoxication with "glycosis." No post-mortem changes were found.—J. K.

(DIABETES) Fats and lipoids in the blood in diabetes mellitus. [Ueber das Vorkommen und die Verteilung von Fetten und Lipoiden im Blute (Plasma) des Menschen bei Diabetes mellitus. Chemische Beiträge zur Kenntnis der Entwicklung und des Aufbaues spezifischer Lipamien. IV.] Fiegl (J.), Biochem. Ztschr. (Berl.), 1918, **90,** 173-214.

Analyses are reported of 100 cases of diabetic lipemia, with regard to technique and distribution of the blood fats and lipoids.—Physiol. Abst. **3,** 576.

(DIABETES) Zur Pathologie und Therapie des Coma diabeticum. Fischer, Deutsche med. Wchnschr. (Leipz. u. Berlin), 1918, **44,** 503.

No new data.—F. S. H.

DIABETES, Fat metabolism in—. Geelmuyden (H. C.), Norsk Mag. for Laegevid (Christiania), 1920, **81,** 479.

Geelmuyden's comparative study of the acute diabetes in pancreatectomized dogs and human diabetes has, he thinks, thrown light on the processes in the intermediate metabolism and their genetic connection, especially in regard to the production of sugar from fat. In research of this kind, he emphasizes, all the changes in the metabolism must be taken into account, not only the glycogen and blood sugar, the glycosuria and the ketonuria, but the migration of fat, the transformation of albumin, the total metabolism and the transformation of energy. Such studies hitherto have been restricted to only some of these elements and their interrelations have been overlooked. He shows that carbohydrates promote the formation of sugar from fat, and that the output of sugar is not increased by feeding fat unless a certain amount of carbohydrate is given with the fat. This he thinks is probably the reason why carbohydrates are so injurious in human diabetes. Diabetes in pancreatectomized dogs seems to be due to the very same anomaly in the metabolism as in human diabetes. The chief difference between them is that it occurs suddenly in the dogs, while in man it is of long, slow development.—J. Am. M. Assn., **74,** 1684.

DIABETES mellitus and complications, Treatment of—. Gilliam (H. A.), Kentucky M. J. (Bowling Green), 1918, **16,** 71-73.

General article containing no new data.—F. S. H.

(DIABETES) Dispensary treatment of diabetes. Granger (A. S.), Calif State M. J. (San Fran.), 1918, **16,** 524-526.

No new data.—F. S. H.

(DIABETES) The influence of menstruation on acidosis in diabetes mellitus. Report of a case. Harrop (G. A.) & Mosenthal (H. O.), Bull. Johns Hopkins Hosp. (Balt.), 1918, **29,** 161-163

An extensive case report, accompanied by urine analyses of a diabetic showing exacerbations during menstruation.

—F. S. H.

(DIABETES) Blood sugar concentration and blood sugar methods. Höst (H. F.), & Hatlehol (R.), J. Biol. Chem. (Baltimore), 1920, **42,** 347-358.

A comparative study has been made of the various methods for the determination of blood sugar; from the study the authors conclude that it is uncertain whether any of the blood sugar methods hitherto used give only the amount of glucose. Bang and Hatlehoel's method and Hagedorn and Jensen's method give in normal individuals and in diabetics values which approximately agree. Folin and Wu's method, as well as Meyers and Bailey's modification of Lewis and Benedict's method, may, at any rate in diabetes with hyperglycemia, give too high results. This is especially the case with the last mentioned method.—F. S. H.

DIABETES, The modern conception of the pathogenesis of—, with special reference to the pancreas (Der jetzige Stand der Pathogenese des Diabetes, mit besonderer Berücksichtigung des Pankreas). Herkimer (Gotthold), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 522-524.

The author believes that the endocrine function of the pancreas is due to the cells of the acini and the cells of the Langerhans islands. But when body cells, especially the islets, are changed by pathological processes diabetes occurs. The islets have no relation with the external secretion of the pancreas. Two cases are shortly described which prove that the liver plays an important part. In these cases the patients with diabetes got cirrhosis of the liver. They lost the diabetical symptoms. In both cases at autopsy, a cirrhosis of pancreas and liver were found.—J. K.

DIABETES; The results of past treatment and future problems. Joslin (E. P.), Bull. Johns Hopkins Hosp. (Balt.), 1918, **29,** 80-85.

A general view of the author's studies accompanied by charts and dietary tables.—F. S. H.

(DIABETES ADRENALS) Acetone in cerobrospinal fluid (Aceton in de ruggemergsvloeistof). Koopman (J.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** 1346-1350.

Acetone may be found in the cerebrospinal fluid in several pathological conditions. During diabetic coma acetone and diacetic acid are found and its pressure is high. When the pressure in diabetes tends to rise it is often significant of approaching coma. Acetone and diacetic acid may be found in the cerebrospinal fluid in diabetic acidosis, also. In a case of adrenal apoplexy it was likewise found.—J. K.

PANCREATIC DIABETES. The alteration of the diastatic activity of the liver and the lack of influence of the glycolytic capacity of muscle on the extirpation of the pancreas in the frog. [Über das Wesen des Pancreas diabetes. (Die Änderung der diastatischen Wirksamkeit der Leber und die Unbeeinflussbarkeit der glykolytischen Fähigkeit des Muskels durch Pankreas- exstirpation beim Frosch)]. Lesser (E. J.), Biochem. Ztschr. (Berlin), 1920, **103,** 1-18.

Induced pancreatic diabetes in the frog causes an increased glycolysis in the intact and isolated liver, while the glycolytic function of either intact or isolated muscles is no different than the normal. No valid conclusion can be drawn concerning the fate of the muscle glycogen from the results of intravenously injected grape sugar for the increase in CO_2 output does not occur if the glycogen content has previously been strongly reduced by hunger and work. The glycogen-poor liver synthesizes glycogen only slightly more rapidly than does the liver containing moderate amounts of glycogen. The fat-sparing action of sugar through the decomposition and rapid synthesis of glycogen in the liver are two coordinated processes, both of which occur only when the glycogen content of the liver passes a certain minimum which does not occur in pancreatic diabetes.—F. S. H.

(DIABETES) Influence of flying on glycemia (Influencia del vuelo sobre la glucemia). Marañón (G.), Siglo Méd. (Madrid), 1919, **65**, 573-574.

In a series of tests made on aviators it was found that an increased glycemia resulted from the flying, caused by the emotional state induced. In the majority of cases the blood sugar values were increased from the normal of 0.09 to 0.12 to values represented by 0.15 to 0.19. In the pilots the hyperglycemia was less, but nevertheless values above the normal were found.
—E. B.

DIABETES and influenza. Motzfeldt (K.), Norsk Mag. f. laegevid (Christiania), 1920, **81**, 372-379.

During the influenza epidemic of 30 years ago diabetes was not infrequently noted in connection with this disease; few observations regarding this have, however, been published during the last epidemic.

Details are given of four cases of diabetes, in which the first symptoms set in during a regular attack of influenza, or shortly afterwards.

The diabetes was of a very mild form in spite of the youth of the patients (age: 35, 14, 15 and 20 years); in 3 of the patients the tolerance for carbohydrates increased considerably during the treatment. Particular interest attaches to case 1: During the course of influenza a man of 35 noticed a peculiar deep epigastric pain. Thirst and polyuria started, when the temperature had been normal for one week. On admission to the hospital one month later the urine gave a positive ferric chloride reaction; the sugar disappeared after 5 days treatment. The tolerance was tested one year and a half later; 500 grams of bread could then be taken without glycosuria. After 50 grams glucose, glycosuria appeared and lasted for 3 hours. The possibility of a pancreatic infection is suggested.—Author's abstract.

DIABETES, Dietetic treatment of serious cases of—(Zur diätetischen Behandlung schwerer Diabetesfälle). Petrén (K.), Deutsche med. Wchnschr. (Berl.), 1920, **46**, 589.

The chief principle in treatment of diabetes is restriction of proteins as well as carbohydrates. Only fat may be taken in unlimited quantities. The results are splendid. Meat is a poison in serious diabetes.—J. K.

(DIABETES) Coma diabeticum during pregnancy. (C. d. bei Schwangeren). Umber, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 589.

It is extremely rare that a pregnant woman dies in diabetic coma. The author saw three cases in which death thus occurred. Two of the patients were known to the author before pregnancy. Both had previously had acidosis, which had disappeared under a dieting regime. In all three cases the fatal influence of pregnancy on the diabetes was obvious.—J. K.

DIABETES innocens. Wynhausen (O. J.) and Elzas (M.). Arch f. Verdaungskrank. (Berlin), 1920, **26,** 33-53.

To decide whether a glucosuria may be considered as diabetes innocens the authors give to their patients on an empty stomach a test breakfast consisting of 150 gms. white bread with a little butter and a cup of tea without sugar or milk. Only these cases may be considered as "innocent" when before and after this test breakfast the blood sugar content is normal or when, after this breakfast, the blood sugar is between 0.15 and 0.17%. The amount of sugar in the urine does not permit a prognosis. Even high glucosuria may be perfectly harmless and accompanied with a normal blood sugar level.—J. K.

(DIABETES INSIPIDUS OSTEOMALACIA) Secretion of iodine in saliva in health and disease after subcutaneous injection of sodium iodide (Jodausscheidung im Speichel bei Gesünden und Kranken nach subkutaner Injektion von Jodnatrium). Zak (E.), Wien. klin. Wchnschr. (Vienna), 1920, **33,** 281.

When sodium iodide is injected subcutaneously it reappears in the saliva on the average in 9 minutes and 40 seconds, in men; in women after 7 minutes and 42 seconds; in men with osteomalacia 5 minutes and 14 seconds; in women with the same disease it appears in 4 minutes and 54 seconds. In osteomalacia the amount of iodine excreted in the saliva is larger than normal. In diabetes insipidus, without treatment, it appeared in about 4½ minutes. Treatment with strychnine lengthened the period to about 10 minutes.—J. K.

DUCTLESS GLAND SUBSTANCES, Influence of certain—on the growth of plant tissues. Budington (R. A.), Biol. Bull. (Woods Hole), 1919, **37,** 188-193.

In an attempt to learn what effects, if any, extracts of the endocrine organs of animals may exert on the growth of plant

tissues, onions were grown upon 120 cc. of Pfeffer's medium to which varying amounts of thyroid, pituitary and suprarenal substances were added. Addition of thyroid substance delayed the growth of the roots, apparently in direct proportion to the amount employed. There was no interference with the growth of the young leaves. Iodine, in the form of KI, did not show this effect. Pituitary and suprarenal substances exerted no appreciable influence.—W. J. A.

DYSTROPHIA MYOTONICA. Maase (O.) & Zondek (A.), Deutsche med. Wchnschr., (Berl.) 1920, **46,** 418.

In this typical case the endocrine symptoms consisted of large nose and lips, polyuria (hypophysis), low blood pressure and a small amount of blood sugar (thyroid), increased salt metabolism and a diminished protein metabolism (thyroid), and sexual impotency.—J. K.

A mass of ENDOCRINE EPITHELIUM in the roof of the mid-ventricle of the Algerian lizard (Amas épithéliaux endocrines dans le toit du ventricule moyen chez un lézard algérien). LeBlanc (E.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 162-163.

In the roof of the ventricle of Uromastix acanthinurus and in the basal region of the epiphysis, there exists, immediately under the ependymal epithelium, a mass of cells which suggests at once an endocrine gland, strikingly like the genital interstitial glands. Other saurians are to be investigated.

—T. C. B.

(ENDOCRINE ORGANS) A therapeutic suggestion concerning endocrines. Bandler (S. W.), Med. Rec. (N. Y.), 1919, **95,** 429-432.

Bandler believes that the future of medicine lies along the lines of endocrine therapy and states that in his own practice 90% of all prescriptions for internal use consist almost entirely if not wholly of endocrine extracts. "The varying forms of amenorrhoea, menorrhagias and metrorrhagias, threatened miscarriage, habitual miscarriage, sterility, the disorders and disturbances of the climacterium, and many other states met with in gynecological practice may be corrected in many instances specifically by a certain extract; in many other cases, by combination of extracts." The author believes that the influenza toxin exerts an almost selective action on the endometrium.

This conclusion is based on observations of the complications of the disease, especially in its sequelae affecting the uterus—which organ he considers lymphoid tissue, part of the thymico-lymphatic system.

Normal secretion and interaction of the ductless glands preserves a proper state of growth, which leads Bandler to believe that the cause of benign and malignant growths will be found in abnormal gland function. He ascribes fibromata and myomata of the uterus to hyperpituitarism of the posterior lobe, with resultant hyperovarianism. He considers hyperactivity of the pituitary as responsible for many premenstrual disturbances. He further theorizes to the effect that in pregnancy, the placental secretion holds in check the menstrual activities of the pituitary, thyroid and ovaries and that failure to inhibit these glands results in habitual miscarriage. The nausea and vomiting of pregnancy are considered as due either to a toxic placental secretion or hyperactivity of the posterior lobe of the pituitary. The use of mammary extract, thymus, or placental extract to overcome hyperpituitarism is recommended, the statement being made that each one diminishes menstrual activity. Glycosuria of pituitary origin is emphasized and is controlled according to the author by mammary, thymus or placental extract. [The article contains many fascinating speculations which are advanced rather positively, but without much concrete scientific evidence to support them. Many of these brilliant theories may prove to be correct, but they cannot as yet be accepted].—H. L.

ENDOCRINE ORGANS, The influence of extracts of—on the secretion of the stomach (Über der Einflusz von Blutdrüsen-extrakten auf die Magensekretion). Boeheim (T.), Archiv f. Verdauungskrankheiten (Berlin), 1920, **26**, 74-120.

The author examined the influence of injected extracts of endocrine organs on the function of the stomach after a Boas-Ewald test breakfast and after a so-called "plasmon breakfast" (15 grams plasmon dissolved in 300 cc. water). The following results were noted.

I. In cases with hyperacidity: After a plasmon test meal injections of extracts of all endocrine organs tend to diminish the quantity of content of the stomach. After injection of thymus or ovary this diminished quantity is only temporary and is followed by an increase. The acidity becomes still higher, though the influence of thymus and adrenalin is not so marked as that of the other extracts. Extract of thymus increases the quantity of peptones in the content of the stomach; the other

extracts, however, increase the quantity of albumoses. After a Boas-Ewald test breakfast all extracts excepting hypophysis increase the quantity of content of the stomach; hypophysis diminishes it. All extracts except thymus diminish the acidity; thymus increases it. Therefore, perhaps in some cases of hyperacidity organotherapy (thyroid or hypophysis) may advisedly be carefully tried.

II. In cases with normal acidity: After a plasmon breakfast thymus and hypophysis increase the quantity of content of the stomach; thyroid and ovary diminish it. Only hypophysis diminishes the acidity. After a Boas-Ewald breakfast all extracts diminish the acidity; thymus, hypophysis and ovary raise the quantity of content of the stomach, thyroid diminishes it. All extracts delay the digestion of proteins.

III. In cases with sub- and an-acidity: After a plasmon breakfast as well as after the Boas-Ewald breakfast injection of extract of pancreas produces a marked rise of acidity. The digestion of proteins goes further than without these extracts. Thymus and thyroid have the same influence. Therefore, these three organs may be tried in such cases. [For earlier observations along the same line see Rogers, Rahe and Ablahadian (Abst. Endocrin., **3**, 231-232)].—J. K.

(ENDOCRINE ORGANS) Experimental basis for organotherapy in infectious diseases (Experimentelle Grundlagen der Organtherapie bei infektious Krankheiten). Borchardt, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 533.

The author examined the influence of various glandular products on the formation of agglutinin for typhoid bacilli. Adrenalin, hypophysin and spermin subcutaneously gave an increase of the agglutinin-titer of the blood serum. Thyroid tablets administered by mouth had the same effect. [See also Koopman, Endocrin., **3**, 318-320.]—J. K.

(ENDOCRINE ORGANS) On the origin and significance of lipase in human blood (Herkunft und Bedeutung von fettspaltenden Fermenten des menschlichen Blutes). Caro (L.), Ztschr. f. klin. Med. (Berlin), 1920, **89**, 49-76.

This article is the report of a study of the influence of disease on the content of lipase in the blood. Adiposity, arteriosclerosis, many cases of Bright's disease and others give an increased lipase content. In the first stage of pulmontry tuberculosis an increase is observed; in the later stages, the lipase content diminishes rapidly. On the other hand, all diseases

with cachexia tend to diminish it. In lymphoid and myeloid leukemia no influence on the lipase was observed. Graves' disease, when accompanied by emaciation, presents a lowered lipase. In myxoedema no effect is observed. Now the question arises as to the origin of the lipase. Bergel has maintained that the lymphocytes produce this ferment. This cannot be true since there is no parallelism between the number of lymphocytes and the lipase content of the blood. This is also true with respect to the cerebrospinal fluid. Probably the lipase is a product of the endocrine system. The author believes that the pancreas plays an important part in its formation. The antagonists of this gland are the thyroid, the chromaffine system, the infundibulum, the ovary, and the thymus. These glands have an important influence on fat metabolism; increased function diminishes the fat in the body; diminished function increase it. Diminished function of these glands increases the internal secretion of the pancreas, which produces a large amount of lipase. When the opposite happens, the pancreatic function is diminished and its influence on the lipase content is demonstrated.—J. K.

ENDOCRINE ORGANS, Functions of—(Wesen und Wirken endokriner Drüsen). Hart (C.), Berlin. klin. Wchnschr., 1920, **57**, 101-104.

The author fed tadpoles with thymus and studied the resulting atrophy of the thyroid. The tissues of the animals showed a swollen aspect which may perhaps have some analogy with the tissue reactions in myxoedema. This is further proof that a monoglandular disturbance is followed by changes in the other organs of the endocrine system and that what appear to be monoglandular diseases are often polyglandular.—J. K.

(ENDOCRINE GLANDS) The use of x-rays and electricity in exopthalmic goitre and other disorders of the ductless glands. Hernaman-Johnson (F.), Arch. Rad. & Elec. (N. Y.), 1918, **23**, 91-99.

Brief case reports and general discussion from which it is concluded that x-rays are specific in the sense that the secretion of the thyroid may be diminished to any required degree, although cure cannot be effected in the face of persistent irritation from any source.

The carefully controlled use of x-rays in dysmenorrhea of ovarian origin is advocated.—F. S. H.

ENDOCRINE ORGANS, The significance of, in the toxemias of pregnancy (Die Bedeutung der innersekretorischen Drüsen für die Klinik der Graviditätstoxikosen). Hofbauer, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 589.

During pregnancy, metabolism is increased. This may be explained by the hyperplasia of thyroid, adrenals and hypophysis. These glands increase the irritability of the sympathicus and parasympathicus. This is perhaps the cause of the vomiting of pregnant women. It may be cured by extracts of ovary, which tend to diminish the irritability of the sympathicus. In eclampsia, the serum of the patients has vasoconstricting properties; the substances with these properties are probably produced by the increased function of the hypophysis-adrenal system. Therefore extract of ovary ought to be tried in these conditions. The edemas and the abnormalities of the kidneys in pregnancy may perhaps be explained by a dysfunction of the hypophysis-adrenal system.—J. K.

(ENDOCRINE ORGANS) The mechanism of vitamine action (Le mecanisme d'action des vitamines). Ganassini (D.) & Mancini (P.), Bull. gén. de Thérap. (Paris), 1920, **171**, 125-133.

A brief review of the physiological, pathogenic and therapeutic action of the vitamines in which the opinion is expressed that their physiological role is to regulate trophic exchanges in synergic connection with the trophic regulatory function of the products of the glands of internal secretion.—F. S. H.

(ENDOCRINE ORGANS) On the decisive proof of the anatomical situation of the glands of internal secretion (Sur les raisons déterminantes du siège anatomique des glandes a sécrétion interne). Hallion (L.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 295-296.

The author claims priority by about ten years, for the hypothesis suggested by Ide, that the role of the endocrine glands can be explained by their embryologic origin (See Endocrin., **4**, 125).—T. C. B.

(ENDOCRINE ORGANS BLOOD SUGAR) Studies in the diastatic activity of the blood and blood sugar curves indicating a decreased carbohydrate tolerance in hyperthyroidism. Killian (John A.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17**, 91-93.

Patients received a breakfast of one egg, two slices of bread and a cup of black coffee or a glass of water. Two hours later the bladder was evacuated and 100 cc. of water drunk. One hour after this a specimen of urine and one of blood were taken as controls. Glucose was then administered in 50% solution, 1.75 gm. per kilo, body weight. At hourly intervals thereafter blood and urine samples were taken and the sugar content and diastatic activity were determined. Twenty-three cases were presented. Three hours after the standard meal the sugar in the blood varied, in normal cases, from 0.09 to 0.10 per cent. In Frölich's dyspituitarism, acromegaly and Addison's disease hypoglycemia was noted. In "hyperthyroidism" (type not specified) the blood sugar ranged from 0.11 to 0.13 per cent. In normal cases urinary sugar excretion ranged from 20 to 30 mg. for the control hour. In dyspituitarism, acromegaly and Addison's disease it was less. In hyperthyroidism, excretion varied from 248 to 95 mgs. In normal cases blood sugar reached its maximum, 0.13-0.15 per cent, in one hour and returned to normal in two hours. In endocrine hypofunction there was practically no increase in blood sugar. In "hyperthyroidism" there was hyperglycemia persisting 4-5 hours, accompanied by glycuresis. Blood diastase was decreased in the hypofunction cases and increased in the hyperfunction.—R. G. H.

(ENDOCRINE ORGANS) Observations on starvation bone-disease in Munich (Beobachtungen von Hungerknochenerkrankungen in München). Mayer, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 168.

The etiology of this disease is considered as a disturbed endocrine balance.—J. K.

(ENDOCRINE ORGANS) Therapeutic problems of the future. Middleton (G. W.), Northwest Med. (Seattle), 1919, **18,** 225-229.

In a general presidential address the author devotes a paragraph to the ductless glands. He refers to the more obvious diseases connected with perversion of the thyroid, adrenal and pituitary body; the neuroses of women associated with ovarian deficiency. The significant advance by Kendall in isolating the crystalline active principle of thyroid secretion is commended. He warns against bizarre commercial pluriglandular prescriptions, but prophesies an important destiny for scientific, dignified organotherapy.—H. L.

ENDOCRINOLOGY, Some phases of. Garretson (W. V. P.), Med. Press (London), 1918, N. S. **105,** 488-491; N. York M. J., 1918, **107,** 866-869.

A general discussion containing no new data save an admission of the conversion of a scoffer (the writer) to an adherence to the practices of endocrinology.—F. S. H.

ENDOCRINOLOGY, The present aspect of—. Lescohier (A. W.), Med. Rec. (N. Y.), 1919, **96,** 532-534.

The author wisely states that "the crying need of endocrinology at present is carefully controlled therapeutic investigation." He objects both to the class of practitioners who are wildly seizing upon organotherapy as a cure-all, and to the class of pessimistic skeptics who barely recognize any place at all for ductless gland therapy. He suggests that gland extracts will probably prove more valuable in the treatment of mild degrees of hypofunction than in outstanding clinical aberrations and accordingly urges that more attention be paid to the recognition of minor deficiencies.—H. L.

FRÖHLICH'S SYNDROME, Case of—(Un nuevo caso de sindrome de Frölich). Crespo Alvarez (A.), Siglo Mèd. (Madrid), 1919, **66,** 713-716.

A detailed history of an interesting case of Fröhlich's syndrome in a boy of 20 years.—E. B.

(GENERAL) The relation of the glands of internal secretion to surgery. Haeberlin (J. B.), Illinois M. J. (Chicago), 1918, **33,** 262-267.

A general discussion presenting no new data.—F. S. H.

(GENERAL) A method for manganese quantitation in biological material together with data on the manganese content of human blood and tissues. Reiman (C. K.) & Minot (A. S.), J. Biol. Chem. (Baltimore), 1920, **42,** 329-345.

While this paper is not primarily of endocrine interest, the data concerning the manganese content of various glands of internal secretion are given and thus made a matter of record.—F. S. H.

(GONADS HYPOPHYSIS) Eunuchoid gigantism (Ein Beitrag zum eunuchoiden Riesenwuchs). Jödicke (P.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berlin), 1918, **44,** Orig. 385-390.

Report of an acromegalic eunuch with high sugar tolerance, the condition being attributed primarily to the sex gland disturbance with resultant hyperfunctioning of the pituitary. —F. S. H.

(GONADS) Eunuchoidismus. Krisch, Deutsche med. Wchnschr. (Leipz. u. Berlin), 1918, **44,** 615.

Rather complete clinical report of two cases of eunuchoidism with no points of particular endocrine interest.—F. S. H.

(GONADS) Hypoplasia of the testicle in youth and its significance as regards the development of the gonads (Ueber die Hypoplasie der Hoden in Jugendalter und ihre Bedeutung für das weiter Schicksal der Keimdrüsen). Kyrle (J.), Wein. klin. Wchnschr. (Vienna), 1920, **33,** 185-188.

Hypoplasia of the testicle in youth is frequent. The hypoplastic organs are characterized by an increased development of the interstitial tissue. During puberty they may develop to a considerable extent but rarely become of normal size. Nevertheless an adequate function is usually present.—J. K.

(GONADS) The psychology and psychopathology of puberty with some remarks on the internal secretions of the sex glands (Zur Psychologie und Psychopathologie der Pubertät nebst einige Bemerkungen über die innersekretorischen Funktionen der Keimdrüsen). Münzer (A.), Berliner klin. Wchnschr., 1920, **57,** 346-349.

A general discussion in which no new data are presented. —J. K.

(GONADS) Hermaphroditism in man. Sheppard (H.), Anat. Rec. (Phila.), 1920, **18,** 259.

A dissecting room case is reported which is held to exhibit true hermaphroditism. Testes, located in the scrotum, and ovaries in the pelvic cavity, were present. The case is an unusual one if, as is stated, both ovaries and testes show a normal structure microscopically.—W. J. A.

(GONADS) Hermaphroditismus. Wagner (G. A.), Wein. klin. Wchnschr. (Vienna), 1920, **33,** 226; Deutsche med. Wchnschr. (Berl.), 1920, **46,** 423.

A description of two cases. The first subject was a "girl" of 16 years with a typical psycho-physical male status. The

penis was short and hypospadic. The scrotum was divided into two parts in one of which there was a testicle, and in the other a cryptorchidic testicle. The second subject was a girl of 21 years who had not menstruated. The characteristics were those of a female both as regards mind and the external genitalia, the clitoris and labia were normal. The vagina was 3 cm. in depth and there were no internal sexual organs. A bilateral herniotomy had been performed, but since a tumor was felt in the old scar a new incision was made and a testicle found therein attached to a normal funiculis. Histological examination of the removed organ showed it to be of normal tissue and containing no traces of ovarian cells.—J. K.

HYPOPHYSIS, The development of the human—. Atwell (W. J.), Anat. Rec. (Phila.), 1920, **18,** 220.

An account is given of the morphogenesis of the human hypophysis beginning with the stage of the 10 mm. embryo. The pars tuberalis, or "lobulus bifurcatus" of Bolk, can be recognized in the younger stages and is then traced continuously to the oldest. It is shown that Herring's "tongue-like process of the pars intermedia" is developed quite independently of the pars intermedia. Thus the name applied by Herring is misleading.—W. J. A.

(HYPHOPHYSIS) Presentation of a case of diabetes insipidus. Clausen (J.), J. Missouri State M. Assn. (St. Louis), 1918, **15,** 189; Proc. Wash. Univ. M. Soc. (St. Louis), 1918, **48,** 8.

C. reports that the injection of pituitary extract invariably caused a marked reduction in the urinary output and thirst, the daily output falling from 7 liters to 2, per diem. The dose given was 0.25 to 1 cc. once a day, and was ineffective when given by mouth.—F. S. H.

(HYPOPHYSIS) The history of a case of acromegaly with gigantism in the family. Craft (M. T.), Neurol. Bull. (N. Y.), 1918, **1,** 32-34.

A very interesting personal report by the patient of the development of the acromegalic condition accompanied by blindness and the statement that a paternal uncle was a famous Kentucky giant.—F. S. H.

(HYPOPHYSIS) The acromegalic tendency and the theory of the internal secretions (Ueber Akromegaliodismus und zur Theorie der inneren Sekretion). Ehrmann (R.), Ztschr. f. phys. u. diätet. Therap. (Leipzig), 1918, **22,** 343-345.

Several observations were made of individuals demonstrating by x-ray examination the classical acromegalic picture, who failed to give marked evidence of hypophyseal disturbance at autopsy. The author theorizes on the absence of the effective secretion from the glandular parts of the adrenals but presents no experimental data.—F. S. H.

(HYPOPHYSIS) A study on the separation of the physiologically active portion of the posterior lobe of the pituitary body. Fenger (F.) & Hull (Mary), J. Biol. Chem. (Balt.), 1920, **42,** 153-158.

This paper reports an attempt on the part of the authors to separate in pure form the oxytocic principle of the posterior lobe of the pituitary. It is concluded on hardly sufficient evidence that the uterus-contracting principle does not occur in the fresh gland in free or crystalline form, but is linked to or part of some protein complex. "In its original protein association the uterine stimulus is insoluble in ether, petroleum ether, chloroform and practically insoluble in absolute alcohol. It is sparingly soluble in 95 per cent alcohol, but yields a highly active split product when treated with hot 95 per cent alcohol. The split product is amorphous in nature, very hygroscopic and much more sensitive to desiccation than the original basic material from which it was derived." Alkaloidal reagents are not sufficiently good precipitants for general use in the isolation of the active principle.—F. S. H.

(HYPOPHYSIS) Case of hypophyseal tumor showing improvement under x-ray treatment (Einen durch Röntgenbestrahlung gebesserten Fall von Hypophysentumor). Fleischer & Jüngling. München. med. Wchnschr., 1918, **65,** 1362.

A report of a case of hypophyseal tumor in a 55 year old woman with acromegalic symptoms and visual disturbances. She was distinctly benefited by 2 x-ray applications at intervals of four weeks. The technique of the applications is given in brief and is not applicable to American made apparatus.

—F. S. H.

(HYPOPHYSIS) Cases of hypophyseal tumor (Fälle von Hypophysentumor). Gerhardt, München. med. Wchnschr., 1918, **65,** 950.

Report of two cases of hypophyseal tumors, one in a 24 year old soldier and the other in a 51 year old laborer. Evidence of acromegaly was present in each case.—F. S. H.

(HYPOPHYSIS) Headache and dyspituitarism in the light of therapeusis. Glassburg (J. H.), Med. Rec. (N. Y.), 1919, **96,** 461-463.

Glassburg emphasizes the desirability of limiting of the term dyspituitarism to exclude acromegaly on the "hyper" side and infantilism on the "hypo" side, but to include all other disorders of pituitary secretions. In this way a definite class of cases can be recognized which may be benefitted by organotherapy, whereas gland extracts are useless in acromegaly and infantilism. Cases of dyspituitarism will show signs and symptoms of both hyper- and hypo-activity depending on the stage of the disease. Dyspituitarism is not necessarily accompanied by an abnormal sella turcica. The author presents a typical case in which the bitemporal headaches, muscular fatigue, etc., were promptly relieved by pituitary extract, 4-8 grains a day by mouth. It was noticed that administration of the extract at the menstrual period resulted in increased flow; the author therefore cautions against using it at that time.—H. L.

(HYPOPHYSIS) A case of acromegalic gigantism (Un caso de gigantismo acromegalico). Gouce (F.) & Poyales (F.), Pediatria españ. (Madrid), 1919, **8,** 271-283.

A report of a girl of eight years afflicted with acromegalic gigantism. The case is very well presented. No glycosuria was present but a slight hyperglycemia was found.—G. M.

(HYPOPHYSIS) A physiological response to the administration of pituitary. Hammett (F. S.), Patten (C. A.) & Suitsu (N.), Am. J. Physiol. (Balt.), 1920, **51,** 588-592.

A study of the changes induced by administration of pituitary substance, in the total nitrogen, non-protein nitrogenous constituents, sugar and alkaline reserve of human blood. The experiments were carried out on six human males who were not endocrinopathic. The period of observation covered nine weeks; the first three weeks no pituitary was fed; during the second three weeks a 2-grain tablet of desiccated pituitary substance was given three times a day; during the last three weeks the pituitary was discontinued. The only valid and consistent change noted was in the blood uric acid. In four out of the six cases the ingestion of pituitary substance caused an increased concentration of uric acid in the blood. This is interpreted as being due, probably, to a decreased permeability of the kidney.—T. C. B.

(HYPOPHYSIS) A case of suspected tumor of the pituitary body. Hansell (H. F.), Trans. Coll. Phys. (Phila.), 1918, 3.s., **39,** 365.

Brief case report presenting no new data.—F. S. H.

(GENERAL) Gastric changes of endocrine origin (Algunas alteraciones intestinales de origen endocrino). Hernando (T.), Med. Ibera (Madrid), 1919, **8,** 239; **9,** 523, also Acad. med.-quir. espan., 1919.

The glands of internal secretion act on the digestive tract through the mediation of the vegetative nervous system indirectly and directly by their secretions. The author studied the endocrine supervision in many cases of diarrhoea and constipation. In all the Basedowians studied diarrhoea frequently occurred and many cases of the latter disorder presented symptoms of hyperthyroidism (18 cases of hyperthyroidism out of 149 chronic diarrhoeas). The intestinal disturbance is explained on the basis of a vagotonia which in turn determines the hyperthyroidism. The same reasoning applies to the occurrence of diarrhoea in many cases of suprarenal insufficiency. As to treatment it should correspond in general with the observed syndrome, belladonna and atropine as moderators of the vagus, and adrenaline (principally as enemas according to de Woorden) which bring about the the least moderating action in an indirect manner exciting the sympathetic. Constipation is also influenced by the endocrine glands. Here hypopituitarism comes into play (the constipation of Fröhlich's syndrome) and in some cases of senile constipation also (atrophy of the hypophysis in the old). Hypersuprarenalism by its sympathicotonic action is a factor. It is possible to understand the constipation of the arterio-sclerotics and the climateric in which ovarian insufficiency plays a role since this also has its effect on vagotonia. Finally there exists a certain group of cases of hyperthyroidism exhibiting constipation in which vagotonia is determined by a condition of the intestinal musculature which is much more frequently found in the cases of hypothyroidism. This intervenes by virtue of a lack of vagal tone and diminution of calcium metabolism, which in turn diminishes the neuromuscular excitation of the intestine.—E. B.

(HYPOPHYSIS) Gigantism (Riesenwuchs). Hoffmann. Deutsche med. Wchnschr. (Berlin), 1920, **46,** 311.

A demonstration of a woman of 21 years with gigantism, multiple exostoses and myxoedematous symptoms of the fatty tissues of the legs. These symptoms developed after a fall 8

years previously, when the hypophysis was injured. No symptoms of a tumor were noted. Sexual functions were normal. The author considers this disorder as due to dysfunction of the pituitary.—J. K.

(HYPOPHYSIS) Akromegalie. Högler, Wien. klin. Wchnschr. 1918, **31,** 769.

A case report presenting no new features.—F. S. H.

(HYPOPHYSIS) Roentgen observation of the pituitary region in intracranial lesions. Johnson (G. C.), Am. J. Roentgenol. (N. Y.), 1918, **n. s. 4,** 555-563.

An extended study with 15 plates of the pituitary region by means of the x-ray. J. concludes that the first requisite for study of intracranial lesions, particularly of the sella, is a wide familiarity with roentgenograms of the normal conditions. There is a wide variation in size and character of the sella which must be considered within the limits of normal. Pituitary struma manifests itself by deformation and destruction of the sella and rarely by visualization of the tumor itself.
—F. S. H.

(HYPOPHYSIS) Hypophysentumor. Killian, Berl. klin. Wchnschr., 1918, **55,** 891.

Of technical interest.—F. S. H.

HYPOPHYSIS, Secretion antecedents in the pars intermedia of the—of the pig. Lewis (D. D.) & Maurer (S.), Anat. Rec. (Phila.), 1920, **18,** 238.

Two kinds of epithelial cells are described for the juxtaneural portion of the pars intermedia. These are: "(1) cells related to the colloid-containing vesicles, and evidently the secretory source of this colloid; (2) the secretory cells which are the characteristic element of the pars intermedia, hitherto vaguely described as finely granular, basophile, neutrophile, etc."—W. J. A.

HYPOPHYSIS, Diabetes insipidus with destruction of the posterior lobe of the— (Diabetes insipidus bei Zerstörung des Hypophysenhinterlappens). Neubürger (K.), Berlin. klin. Wchnschr., 1920, **57,** 10.

A description of a case of diabetes insipidus with a metastatic cancer in the pars nervosa. The anterior lobe showed no changes.—J. K.

(HYPOPHYSIS) Hypophyseal adiposity in children (Ueber Kinder mit hypophysärer Adiposität.) Peritz, Berlin. klin. Wchnschr., 1920, **57**, 379.

The most ordinary cause of hypophyseal adiposity in children is a syphilitic hydrocephalus. Blood sugar is often increased. The author demonstrated some of these cases and also a case of hypophyseal dwarfism, caused by syphilis.
—J. K.

(HYPOPHYSIS) Akromegalie. Pribram, Deutsche med. Wchnschr, 1920, **46**, 424.

This classical case was remarkable because of its beginning during puberty.—J. K.

HYPOPHYSIS and Raynaud's disease (Hypophyse and Raynaudscher Krankheit). Pribram, Berlin. klin. Wchnschr., 1920, **57**, 67.

Data reported elsewhere. See Endocrin., 1920, **4**, 279.
—J. K.

The HYPOPHYSIS cerebri of the American marmot (Marmota monax) with special reference to changes during hibernation. Rasmussen (A. T.), Anat. Rec. (Phila), 1920, **18**, 255.

The author has not found the marked changes in the hypophysis which other writers have reported as taking place during hibernation. The most constant and striking alteration occurs after waking up when the basophilic cells become very promient and show large vacuoles and a conspicuous "macula."
—W. J. A.

(HYPOPHYSIS) Pituitary feeding and egg production in the domestic fowl. Simpson (Sutherland), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17**, 87-88.

Clark in 1915 reported that feeding desiccated hypophysis resulted in marked increase in egg laying by hens. Simpson repeated Clark's experiments, using hypophysis from both adult and young cattle. The experiments were made in three stages: when egg laying was low and declining, when it was

at its height and again when it was low. White Leghorn hens were used as experimental animals. The results were completely negative, not only with the dosage used by Clark (the equivalent of 20 mg. fresh gland) but also with double and treble this dosage.—R. G. H.

HYPOPHYSIS, The action of extract of—on the distribution of the blood (Die Wirkung der Hypophysesextrakte auf die Blutverteilung). Rosenow, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 559.

Intravenous injection of extract of hypophysis produces in normal individuals a momentary increase of the volume of the arm, as may be proved by use of the plethysmograph. This may be explained by the constricting effect of hypophysis extract on the blood vessels innervated by the splanchnic nerves. The author recommends this method for the functional study of the splanchnics.—J. K.

HYPOPHYSIS, A biological study of the—. Saito (T.), Sei-I-Kwai M. J. (Tokyo), 1919, **38,** 328 (Japanese).

The chief points indicated in this paper are that the weight of the hypophysis of the horse varies with the month of the year; that it is relatively much larger in the horse than in either the cow or man, and that its weight decreases during the fourth month of pregnancy in the horse and during the third month in man.—E. V. C.

(HYPOPHYSIS) Cure of a case of meningitis after endonasal operation for hypophyseal tumor by trypaflavine infusions (Heilung einer Falles von Meningitis nach endonasaler Operation eines Hypophysentumors durch Trypaflavininfusionen). Spiesz (G.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 207-209.

Of no immediate endocrine interest.—J. K.

(HYPOPHYSIS) Contribution to the pathogenesis of dystrophia adiposo-genitalis (Bydrage tot de pathogenese der dystrophia adiposo-genitalis). Stenvers (H. W.), Nederl. Maandschr. Geneesk. (Leiden), 1920, **1,** 45-60.

Stenvers describes three cases of dystrophia adiposo-genitalis. The first case was a girl of 17, without menstruation, with adiposity. The diagnosis was tumor of the hypophysis. Death followed some hours after operation. At autopsy the

hypophysis proved to be normal, both grossly and microscopically, but the infundibulum of the third ventricle was very atrophic. The second case was a girl of 21; the menses had become irregular and finally ceased. There were symptoms of brain pressure. The skiagram showed an enlarged sella. The post-mortem examination disclosed a normal hypophysis and a large tumor in the right temporal lobe of the brain with dilatation of the third ventricle. In this case there was no adiposity, but the changes in the third ventricle were not so great as in the first one. The third case, a boy of 14, had headache, giddiness and vomiting. There were eye symptoms. During two years the boy became fatter and fatter and acquired a female form. The skiagram showed changes which may be explained only by dilatation of the third ventricle. These changes developed pari passu with the adiposity. The author concludes that dystrophia adiposo-genitalis is caused by a disease of the third ventricle; this may be caused by a tumor of the hypophysis, but also by any process causing increased intracranial pressure. [An obvious comment is that cerebral pressure may result in functional inadequacy of the hypophysis as well as hypophyseal tumor cause cerebral pressure.]—J. K.

(HYPOPHYSIS) Paroxysmal nasal hydrorrhea based on dyspituitarism. Strauss (S. G.), Med. Rec. (N. Y.), 1919, **96,** 463-464.

Strauss records case of periodic discharge of copious colorless mucous from nose, 2 months after striking forehead against a door. Discharge would last about 6 weeks, then suddenly cease, to reappear in 3 months. Physical characteristics of patient suggested dyspituitarism and whole pituitary gland was administered with prompt and so far (6 months) permanent relief.—H. L.

(HYPOPHYSIS) Atrophia adiposo-genitalis. van Valkenburg (C. T.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** (i), 997-998.

A description of a case of a boy 14 years old with symptoms of meningitis, dullness, epilepsy, Argyll-Robertson pupil, negative Wassermann reaction, optic neuritis, no changes in urine or blood, loss of memory and confabulations. The testicles were small. The patient gradually became more fat. Post-mortem examination showed tubercles in the cerebellum, tuberculosis of the pia-mater, infundibulum, optic nerves and tract, also a large thymus, small pancreas, atrophic testicles,

atrophic adrenal medulla and a normal thyroid, parathyroid and hypophysis were noted. The blood vessels in the latter were increased in number and were congested.—J. K.

(HYPOPHYSIS) The relations between experimental polyuria after "piqure" and diabetes insipidus (Die Beziehungen der experimentellen Piqure—polyurie zum Diabetes insipidus). Veil, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 558-559.

The author describes two classes of diabetes insipidus, one in which the blood contains an increased amount of Na Cl and one with a normal amount of NaCl in the serum. In the first cases the urine is poor in NaCl, in the latter there is generally hyperchloruria. "Piqure" in the fourth ventricle produces polyuria with an increase of NaCl in the urine; "piqure" in the midbrain produces polyuria with hypochloruria.—J. K.

(HYPOPHYSIS) Dystrophia adiposo-genitalis, with report of a case. Whyte (G. Duncan), China M. J. (Shanghai), 1920, **34,** 139.

A typical case is reported in a man of 46 years which showed only temporary improvement on feeding hypophysis. —E. V. C.

(HYPOPHYSIS ADRENALS) Prophylaxis of paralysis of the intestines (Zur Verhütung der Darmlähmung). Zondek (B.), Zentralbl. f. Chir. (Leipzig), 1920, **46,** 270-272.

Unger has advised the administration of asthymolysin after operations as a prophylaxis against paralysis of the intestine. Asthymolysin is a combination of 40 milligrams hypophysis and 0.8 milligrams adrenal. Zondek calls this a bad combination as hypophysis will increase the tonus of the intestine, but adrenaline will inhibit the peristalsis by stimulation of the sympathic apparatus.—J. K.

(INTERNAL SECRETIONS) The importance of a knowledge of the internal secretions and its availability for practical gynecology (Die Bedeutung der Lehre von der inneren Sekretion und ihre Nutzanwendung für die praktische Gynäkologie). Aschner (B.), Monatsch. f. Geb. u. Gynäk. (Berlin), 1920, **51,** 130-136.

A polemical reply to H. Fehling's article of the same title (idem. **50,** 143) and defending the author's book, "Die Blut-

drüsenerkrankungen des weibes und ihre Beziehung zur Gynäkologie und Geburshilfe." (Wiesbaden, Bergmann, 1918). —F. S. H.

INTERNAL SECRETIONS, Influence of—on the formation of bile. Downs (A. W.), Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt), 1920, **51,** 193-194.

See Endocrin., 1919, **3,** 214.

INTERNAL SECRETIONS, Vitamines and—(Vitaminen en inwendige afscheiding). van Driel (B. M.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** (i), 1350-1361.

A general review without new data. The author concludes that the avitaminoses are closely related to endocrine disturbances because in all such conditions the endocrine organs (with the exception of the hypophysis and the adrenals) are atrophied, and because in certain forms of the disorder the amount of adrenalin in the adrenals is increased.—J. K.

INTERNAL SECRETIONS, The. Friedman (E. D.), Med. Rec. (N. Y.), 1919, **96,** 916-935.

The author's intention apparently was not to present anything new, but to compress into ten pages a resume of our knowledge of the internal secretions. He has packed an extraordinary amount of information into this article, including a historical survey. He then crowds an immense amount of information under the headings: thyroid, hypophysis, adrenals, pineal, thymus, sex glands, internal secretions, uterus, parathyroids, pancreas, internal secretion of the alimentary tract, placenta and spleen. It is obviously impossible to abstract this paper, for it is a veritable abstract in itself. It might be recommended to those unfamiliar with endocrinology, who might desire a rapid introduction to its essential features. —H. L.

INTERNAL SECRETION, Feeding rats on glands of—. Gudernatsch (J. F.), Anat. Record (Phila.), 1918, **14,** 35. (Proc. Am. Assn. Anat., 1917.)

Gudernatsch reports the results up to the time of going to press of feeding seven sets of albino rats on a mixed diet plus desiccated thyroid, thymus, hypophysis, testicle, ovary, and mammary gland respectively, one set being used for control. Thyroid fed rats when pregnant deliver many dead, or the young die early. The remaining rats are classed in three

groups: 1. Hypophysis; thymus. 2. Normal. 3. Testicle; ovary. The animals in group 1 grow faster and the animals in 3 slower than normally. Testicle- and ovary-fed homologous animals do not live as long as the others and a decline in weight often begins as early as seven months. Heterologous testicular and ovarian feeding causes an improvement in growth over the homologous fed animals. The members of group 1 are fine breeders and the young are viable. Females of group 3 are poor breeders in respect to the vitality of the young. Pituitary fed animals seem to be precocious in adolescence.—F. S. H.

INTERNAL SECRETIONS, Pernicious anemia and the—. Schauman (O.), Finska. Läk. Sällsk. Handl., 1919, **61**, 796-827.

The author calls attention to certain critical constitutional impulses which may precede anemia. They are primarily achylia, dental caries, and glossitis. He further points out that there are certain points of similarity between Addison's disease and pernicious anemia, such as bronzing of the skin; in certain cases extraordinary good condition of nourishment, stomach and intestinal symptoms of like nature, etc. Among other symptoms present in pernicious anemia significant of an endocrine possibility are polyuria, cardiac enlargement, temperature increases of a peculiar kind, etc. It is also emphasized that the blood changes in themselves may be considered as of an internal secretory nature. The disturbances of the internal secretory balance combined with constitutional anomalies of the hemopoietic apparatus are the fundamental causes, the exogenous influences are but the adventitious motivations of the disease.—J. A. H.

LIPODYSTROPHIA PROGRESSIVA, Sequel of the case of— shown on January the 24th, 1919. Weber (F. P.) and Gunewardene (T. H.), Brit. J. Child. Dis. (Lond.), 1920, **16**, 200-204.

The authors present the findings in what they claim to be the first published autopsy in lipodystrophia progressiva. Their patient was a girl of 13 who died from chronic pyemia. The body was wasted, but by naked eye examination the fat was practically completely absent from the subcutaneous tissue of the upper part of the body above the pelvis. A moderate amount of fat was present in the gluteal regions, orbits, omentum, about the kidneys, heart and pericardium and under the serous membranes. Microscopic sections of the scalp and abdominal wall show that fatty tissue is almost completely, if

not completely, absent. One of the sections of the suprarenal glands included a little of the surrounding retroperitoneal tissue. Definite fatty tissue was present in this. In no section were there lobules of embryonic fatty tissue such as are found in the fetus and in infants. No abnormality was found in either the ovary or pituitary body. In the suprarenal bodies there appeared to be less lipoid tissue than usual, but the effect of the infection which caused death cannot be excluded. In the thyroid there was an excess of colloid of a degree, however, that is often found at autopsy. It fell far below that which frequently occurs at puberty. Little significance could be attached to this excess of colloid if it were the only unusual feature, but it appeared to be associated with fibrosis and an actual diminution in the size of the gland. The thymus gland was represented by a scanty remnant. Original report of this case abstracted in Endocrin., 1920, **4**, 138.—M. B. G.

MENSTRUATION AND PREGNANCY, Disorders of—after accidents [Menstruations und Schwangerschaftsstörung nach Unfall (Verbrennung)]. Beckey (K.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttgart), 1920, **82**, 257-283.

Of no endocrine interest.—F. S. H.

Vicarious MENSTRUATION (Über vikariierende Menstruation). Roth (A.), Monatschr. f. Geburtsh. u. Gynäk. (Berlin), 1920, **51**, 41-57.

A statistical presentation, of no specific endocrine interest. —F. S. H.

MYOTONIA, Variations of—(Varietäten der Myotonie). Kastan, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 311.

Of no endocrine interest.—J. K.

MONGOLISM, The symptoms of— (Zur symptomatik des mongolismus). Moro, München. med. Wchnschr., 1920, **67**, 360.

Data reported elsewhere.—J. K.

(ORGANOTHERAPY) Ductless gland therapy. Masterman-Wood (J. L.) and Torquay (L. M.), Practitioner (Lond.), 1919, **102**, 259-270.

The author believes firmly in careful clinical experimentation in opotherapy, in addition to laboratory investigations,

and believes that the practicing physician may thus help to shed light on what is yet to be discovered in the domain of endocrinology.

Taking up hypothyroidism he emphasizes the inability of the thyroid in this condition to react to iodides or to metabolize iodides brought to it. This condition frequently follows acute infections. In the secondary constitutional stage of syphilis, the thyroid is profoundly depressed and iodides medication is consequently ineffective until the thyroid has recovered. Reference is made to the interesting experience of Rendle Short, who states that he has found thyroid extract quite as effective as iodide of potassium in healing tertiary syphilis. He therefore recommends thyroid extract where iodides fail. Some toxemias do not inhibit the thyroid, but stimulate it to increased activity, as in early tuberculosis. Some of the symptoms of tuberculosis are sympatheticotonic and resemble those of Graves' disease. The authors suggest that in children, adenoids, nocturnal enuresis, slight want of mental alertness, sluggish bodily movements, slightly sleepy appearance of the eyes, sluggish bowels and foetid stools, and a tendency to develop flat foot are sometimes indicative of hypothyroidism and are markedly relieved by small doses of thyroid extract. A case of asthma is cited which was relieved by thyroid extract. An ingeneous hypothesis is constructed to explain this phenomenon. They believe that the vagus is exerting a preponderant influence, inducing bronchial spasm and that thyroid extract stimulates the suprarenals, which in turn stimulate the sympathetic system and overcome the vagus spasm. The wonderful efficiency of adrenalin in attacks of asthma corroborates this viewpoint. Other cases of sub-thyroidism are cited, in which administration of thyroid extract was efficacious. They stress the importance of recognizing mild degrees of thyroid deficiency. The article is suggestive, but not entirely convincing.

—H. L.

ORGAN EXTRACTS. Note on the use of—in place of virulent blood in immunization and hyper-immunization against rinder-pest. Boynton (W. H.), Philippine J. Sc. (Manila), 1918, **13**, Sect. B, 151-158.

Of no endocrine interest.—F. S. H.

ORGANOTHERAPY in certain diseases of childhood. McCready (E. B.), Med. Rec. (N. Y.), 1919, **96**, 529-532.

A large part of the article is a tribute to Sajous' doctrines in the domain of the ductless glands. The rest of the paper

contains much of general matter not readily abstacted. The author concludes that the endocrine glands control metabolism and preside over growth and development in infancy and childhood; they are essential to mental, physical and reproductive efficiency in adult life, and they maintain metabolic balance in the period of decline. Many diseases and conditions of childhood are manifestations of organic inferiority in the etiology of which dysfunction of the endocrine glands is a more or less prominent and contributing factor. Treatment directed toward the stimulation, modification or correlation of the action of the endocrine glands is a promising field of therapeutic endeavor, but treatment by organotherapeutic preparations should be preceded by a careful analysis and evaluation of the symptoms of endocrinous dysfunction. The usually employed doses of organic preparations, particularly of thyroid, are too large, are administered without due care, often in unsuitable cases, and tend to discredit a valuable therapeutic measure.—H. L.

(OSTEOMALACIA) Statistical observations on the increases in rickets and osteomalacia in Berlin (Statistische Bemerkungen zur Frage der Rachitiszunahme und des Auftratens der Kriegsosteomalazie in Bereiche von Gross-Berlin). Engel (H.), Berlin. klin. Wchnschr., 1920, **57**, 35.

Of no immediate endocrine interest. [In the German literature at the present time are appearing various articles on osteomalacia, postulating endocrine factors. To forestall lost effort on the part of those interested, the endocrine bearing of each will be indicated.—Ed.]

OVARY, Observations on the follicular atresia in the rabbit. Asami (G.), Anat. Rec. (Phila.), 1920, **18**, 323-343.

In the rabbit atresia has been observed to occur in the small as well as in medium and large size follicles. In the case of the medium and large follicles the primary factor is the degeneration of the granulosa, while in the early stages of atresia of small follicles changes occur in the egg as well as in the granulosa, and of these the changes in the egg are the more pronounced. These atretic processes do not show any definite relation to the sexual cycle such as occurs in the guinea pig. The article is not primarily of endocrine interest, but attention is drawn to Loeb's suggestion that the normal proliferation of the granulosa is probably dependent upon an internal secretion of the ovum which acts as a growth stimulus.

What the primary cause of the observed atretic changes may be constitutes an interesting question possibly of endocrine portent.—W. J. A.

(OVARY) Ovarian insufficiency as a probable cause of epilepsy. Ashe (J. S.), Dublin J. Med. Sc., 1920, **4**, 142.

Ashe cites three cases of patients that have been benefited by ovarian administration. In one following a bilateral tubal pregnancy, menstruation ceased entirely. Concomitant with this the subject had what the author designates "hystero-epileptic attacks." Injections of the fresh fluid extract of ovarian tissue stopped these attacks. Epileptic attacks in another case followed an attack of mumps. Feeding of ovarian tissue stopped them. In a third case a polyglandular mixture, including ovarian substance, decreased the attacks. It is suggested that the toxin which serves as a predisposing factor in certain cases of epilepsy is produced by absence, diminution or change in the ovarian ferments leading to some polyglandular deficiency. The imbalance thus set up leads to the production of toxins which act on the cerebral cortex, causing the epileptic seizures.—J. H. L.

OVARY, Precocious puberty due to tumor of the—(Genitalismo precoz por tumor ovarico). Cortiguera (J.) & Lopez Albo (W.), Rev. de pediat, 1919, —, —.

A report of a girl of 10 years who had menstruated since 6 years of age. She was born with much hair on her head and an early development of somatic and mental characteristics was noted out of proportion to her years. At eight months she cut her first teeth. Her physical appearance was that of a person of 20 years (pubic hair, developed mammae with colostrum, etc.). Her abdomen was enlarged as if she were in the sixth month of pregnancy. Palpation gave evidence of a smooth, spherical and movable tumor underneath the skin. A laparotomy was performed and an ovarian tumor found.—E. B.

OVARY, On an anomaly of development of the—in Ascaris megalocephala (Sur une anomalie du développement de l'ovarie chez l'Ascaris mégalocephala). Dragoiu (J.) & Faure-Fremiet (E.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 123-124.

A histological description of the ovaries and genital tract of a sterile female.—T. C. B.

OVARY, Pathological pregnancy and tumors of the—(Pathologische Schwangerschaft und Eierstocksgeschwülste). Fraenkel (L.), Berlin. klin. Wchnschr., 1920, **57**, 1-3.

Of no immediate endocrine interest.—J. K.

(OVARY) The time of ovluation (Het tijdstip der ovulatie). van der Hoeven (P. C. T.), Nederl. Maandschr. v. Geneesk. (Leiden), 1920, **1**, 16-22.

Of no endocrine interest.—J. K.

(OVARY) Rythmical recurrence of the typical oestrus cycle after ovarian transplantation. Long (J. A.) & Evans (H. M.), Anat. Rec. (Phila.), 1920, **18**, 245.

Successful transplantation of the ovaries in the rat has been accomplished by the authors in 14 instances. In most successful cases the first interval after the operation was only slightly longer than the dioestrous interval of normal cycles. Sections show that such transplanted ovaries are essentially normal in containing healthy and atretic follicles, corpora lutea of several ages, and interstitial tissue.—W. J. A.

(PANCREAS) Hemorrhagic pancreatic necrosis and diabetes with acidosis (Ausgedehnte hämorrhagische Pankreasnekrose und Diabetes mit Acidose). Caro & Winkler, Deutsch. Arch. f. klin. med. (Leipzig), 1918, **125**, 147-159.

A detailed clinical, post-mortem and histological description with plate of one case of hemorrhagic necrosis of the pancreas accompanied by diabetes with acidosis.—F. S. H.

(PANCREAS) A consideration of the surgical hazards in diabetic patients. Foster (Nelles B.), Ann. Surg. (Phila.), 1920, **71**, 382.

This paper is based upon a review of the clinical records of two good hospitals. Glycosuria is not a reliable guide in the estimation of the severity of diabetes. The disease, however, can be diagnosed and its severity estimated by a determination of the degree of hyperglycemia. Infections tend to increase the severity of the disturbance of carbohydrate metabolism and, in that way, to bring about a variable degree of acidosis. Anesthetics, and especially ether, intensify the disordered processes. Based upon his experience, it is the author's opinion that a case with a CO_2 combining power of its plasma of less than 40 does not present a reasonable margin of safety for

surgical procedures. The author outlines his preoperative treatment and dietetic management of cases of diabetes mellitus. The object of this treatment is the restoration of normal metabolism and its success is measured by the blood sugar and CO_2 combining power of the plasma.—J. F.

(PANCREAS) Reply to Albu concerning the diagnosis of pancreatic cysts (Bermerkung zu Albu: Zur Diagnostik der Pankreaszysten). Holzknecht (G.) & Jonas (S.), Berl. klin. Wchnschr., 1918, **55,** 582.

Of technical interest.—F. S. H.

PANCREATIC DIABETES, The pathology of—(Das Wesen des Pankreasdiabetes). Lesser, Berl. klin. Wchnschr., 1920, **57,** 310.

Data reported elsewhere. See Endocrin., **4,** 296.—J. K.

(PANCREAS) Some remarks on the blood sugar in diabetes mellitus. Lindblom (S.), Hygiea (Stockholm), 1919, **81,** 753-759.

In diabetes the ability to regulate the relation between production and consumption of sugar, so that equilibrium obtains without glucosuria, is arrested or destroyed. In this case there must of necessity be a higher blood-sugar content than is compatible with the kidney permeability, so that the organs or eventually their centers react with a decreased production or an increased destruction. The hyperglycemia present in diabetics acts then in opposition to the metabolic disturbance. Hyperglycemia is then in a certain degree an advantageous symptom. According to this conception the urine of many diabetics does not become sugar-free in spite of the residual hyperglycemia but because of it. The favorable action of the oat-cure is explained on the basis of the suddenly increased hyperglycemia.—J. A. H.

PANCREAS and diabetes mellitus, The relation between the—(Die Besiehungen des Pankreas zum D. m.). Seyfarth, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 589.

The author does not believe that the islands of Langerhans are special organs related to carbohydrate metabolism. It is not true that in diabetes only the islets have undergone pathological changes; at least it has never been proved. For the development of diabetes it is necessary that large parts of the

gland be destroyed and that this pathological process proceeds so rapidly that regeneration is impossible.—J. K.

(PARATHYROID) Parathyroid studies. I. The normal anatomy of the parathyroid glands. Bergstrand (H.), Acta. Med. Scand. (Stockholm), 1919, **52**, 791-856.

These studies were made on human material. A follicular arrangement of the gland cells was found, at times the follicles being grouped in actual glandular nests with lumena. With Bielchowski's stain a hitherto unknown lattice net work was brought out, the fibrils of which surround the capillaries and extend out through the follicle, binding together the individual parenchyma cells. There is only one type of cell present, the so-called chief cells. The "achromatic protoplasm" of these cells is an empty space produced by shrinkage. The granules of the cells are artefacts which have arisen through the precipitation of the protoplasmic net by fixation. The cells of Welsh are degenerated chief cells, their eosinophilia is not concerned with granules. However, there are present in these cells granules of another type, which have been established as fat granules and unrelated to the colloid formation. The parathyroid cells are quite rich in fat granules: the fat is stable, gives the reactions for neutral fat, and is neutral. The colloid arises partly through degeneration of the Welsh cells and partly by secretion from these cells as from the chief cells. The so-called "eosin red components" are formed of the normal intercellular secretion. The interstitial tissues contain large deeply granulated cells with long processes and large vacuoles. The granules show the same metachromatic properties as the histogenic mastcells, but give, however, a positive test with Schulze's oxidase reaction in differentiation from the latter. Perhaps they are identical with Erdheim's pigment cells.—J. A. H.

PARATHYROIDS, Therapy of postoperative tetany (Zur Therapie des postoperativer Tetanie). Borchers (E.), Zentralbl. f. Chir. (Leipzig), 1920, **46**, 293-297.

The only treatment of postoperative tetany is transplantation. Of course, one may see failures, but other treatment has never succeeded. Especially administration of parathyroids by mouth has no effect. The best organs for transplantation are fresh parathyroids from children dying during accouchement.

—J. K.

(PARATHYROIDS) On the origin of the muscular tremors, clonic and tonic spasms in parathyroid tetany. Luckhardt (A. B.), Sherman (M.) & Serbin (W. B.), Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51,** 187.

Parathyroidectomy was performed in dogs after they had recovered from transections of the cord at various levels. Without transection the neuromuscular phenomena are less severe in the hind limbs than in the fore limbs. With transection the fibrillary contractions occur posterior to the transection; may be present in the hind limbs independently of the fore limbs; may persist in the hind limb when its musculature is isolated. Clonic spasms persist. Tonic spasms are less pronounced. There is a great increase in reflex irritability just prior to and during an attack of tetany, followed by a corresponding nervous depression after the attack. Graded doses of strychnine can produce a condition not to be distinguished from tetany. Experiments on dogs seem to show that the cerebellar arc reinforces, but does not initiate the tonic spasms.

—T. C. B.

PINEAL tumor, A case of— (Een geval van gezwel van epiphyse). Hekman (J.), Med. Tijdschr. v. Geneesk. (Haarlem), 1920, **64** (i), 1891-1893.

A girl of 14 years had, when she was 3, fallen from a chair striking her head on the floor. Of recent years her sight has become worse and worse, and she has become very fat. From time to time she has epileptiform attacks. Menstruation began at 11. The child is very erotic. There are neurological symptoms of an old encephalitis in the neighborhood of the capsula interna (paresis of left arm and leg with high jerks; Babinski's symptom, etc.). Both eyes show an optic neuritis. The fatness, the increased sexuality and the eye symptoms may be considered as evidence of localization of the etiologic process in the pineal gland.—J. K.

(PITUITARY) Demonstration of an apparent one-sided acromegaly (Demonstration einer schienbar halbseitige Akromegalie). Biedl (A.), Wien. klin. Wchnschr., 1918, **31,** 487-488; Med. Klin. (Berlin.), 1918, **14,** 577-579.

A description of a case of one-sided acromegaly presented before the scientific association of German physicians in Bohemia. The acromegalic phenomena were exhibited on the left side in all their usual distinctiveness. No enlarged sella turcica was observed under x-ray examination. The anamnesis

records a gradual enlargement of the left arm beginning in the fourth year. The existing complaint was sudden loss of vision, pain in legs, fever, and anuria, which were regarded as due to acute meningeal or cerebral disturbance. No satisfactory explanation of the unilateral growth is given.—F. S. H.

(PITUITRIN) Labor with special reference to pituitrin, morphine and instruments. Harrison (A. G.), J. Arkansas M. Soc. (Little Rock), 1918, **14**, 211-212.

Cautions against the indiscriminate use of pituitrin in labor.—F. S. H.

(PLACENTA OVARY) Substances that increase the growth of the sexual organs (Ueber Substanzen die das Wachstum des Genitale wirksam anregen). Schroeder, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 417-418.

The opinion is expressed that infantilism in women is caused by hypofunction of the ovaries. The author tried the influence of extracts of various organs on the genitalia. From an ether-acetone-alcohol extract of the placenta he obtained a cholesterin-like substance which when injected daily into young rabbits in doses of from 0.3 to 0.5 grams caused hypertrophy of the muscles and mucous membrane of the vagina and uterus. The influence of the ovaries and fallopian tubes was slight. When the same procedure was carried out with males the utriculus masculinus responded by hypertrophy, while the effect upon the epidydimus and penis was negligible. The extracts seem to be effective even when diluted to one-fiftieth. Extracts from other organs were tried but, with the exception of the liver, gave uniformly negative results. Commercial preparations of the ovary were without effect.—J. K.

POLYGLANDULAR DISORDER (Pluriglanduläre Erkrankung). Pribram, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 424.

A demonstration of a 26-year-old girl who had complained for three years of headache, goitre, and cessation of menstruation. Two years previously strabismus set in with diplopia. The fingers became thicker. A strumectomy was performed. At present there is hemianopsia, insufficient power of renal concentration, an enlarged sella turcica, claw-like hands and hypoplasia of the genitals. After the removal of an adenoma of the hypophysis the eye symptoms improved, but diabetes developed. This case is characterized as a diseased condition of the thyroid, hypophysis, pancreas, and ovaries.—J. K.

(PROSTATE) The action of prostatic extracts on isolated genito-urinary organs. Macht (David I.) & Matsumoto (S.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17**, 102-103.

The action of prostatic extracts on the contractions and tonicity of uterus, fallopian tube, bladder, vas deferens and seminal vesicle was studied in vitro. Extracts were made from ram's, dog's, bull's, steer's and human prostates. All the tissues mentioned were stimulated, the uterus and fallopian tube with least quantities, bladder and uterus, next, and vas deferens and seminal vesicles requiring the largest amounts. It was concluded that prostatic extracts have no specific or marked influence on the tonus and contractions of the bladder,—at least, under the conditions of the experiments reported. A more extensive report is to appear in the Journal of Urology.—R. G. H.

PROSTATE, The action of extracts of the—on the isolated genito-urinary organs. Macht (D. I.) & Matsumoto (M.), Proc. Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51**, 203.

The uterus, fallopian tube, bladder, ureter, vas deferens and seminal vesicle are all stimulated in vitro by aqueous extracts of mammalian prostate, including the human. Different organs require different doses. The conclusion is that prostatic extracts can not be regarded as having any specific influence in vitro on the tonus and contractions of the bladder.

—T. C. B.

PUBERTY (La pubertad). Blanc Fortacin (J.), Soc. Españ. de Obst. y Ginec., 1919, ——, ——.

Puberty is considered in its physiology and its pathology as an endocrine event in which the secretions of the genital glands, the hypophysis, the thyroid and the suprarenals take part as excitants of the sexual development while the thymus and the pineal act as inhibitors. The harmonious action, reaction and interaction of the endocrine system determines the successful pubertal development; a disturbance in the balance results in the evolution of a pathological condition.—E. B.

(SPASMOPHILIA) Case of spasmophilic diathesis, with some remarks on the types of convulsions occurring during the suckling period. Wirseen (J.), Hygiea (Stockholm), 1919, **81**, 992-997.—J. A. H.

(TESTIS) Spondylitis rhyzomelica (of Marie-Strümpell). Hertzberger (L.), Inaug. Dessertation, Amsterdam, 1920.

The author considers "spondylitis rhizomélique" as due to gonadal dysfunction. It is much more frequent in men than in women. The subjects are nearly always sterile. In some respects the disease resembles osteomalacia but differs among other ways in that it is characterized by high calcium content of the bones. Osteomalacia is often seen in localities where Graves' disease is common, whereas, in Holland the spondylitis is rather frequently seen in the Friesland district, where myxedema is the common thyroid disorder. In spondylitis rhyzomélique, the administration of ovarian preparations leads to marked augmentation of excreted phosphates and urates. The thesis is further supported by the arguments that the sex-glands are known to have an important relationship to osteogenesis and that in the subjects of this malady a history of gonorrhea is often obtainable.—J. K.

(TESTIS) Induced testicular degeneration and accompanying hypertrophy of the interstitial tissue. Kuntz (A.), Anat. Rec. (Phila.), 1920, **18**, 137.

Experimental evidence is presented to show that hypertrophy of the interstitial tissue in the testis occurs more promptly as an accompaniment of degeneration of the seminal epithelium than as a compensation process. In the series of operated dogs reported bilateral degeneration of the testis followed unilateral vasectomy with occlusion of the duct. In unilateral castration the testis on the unoperated side showed no evidence of degeneration.—W. J. A.

(TESTICLE) Myotonische Dystrophie. Minkowski, Berl. klin. Wchnschr., 1920, **57**, 234.

Dystrophic myotonica is a polyglandular disease. The author demonstrated a case with cataract and atrophy of the testicles.—J. K.

TESTICLE, Tissues of the—and avitaminosis (Tessuto testiculare ed avitaminosi). Novaro (P.), Gazetta degli Ospedali (Milano), 1920, **41**, 424.

The author observed that pigeons fed on a diet without vitamine B show degeneration of the epithelium of the tubuli testiculari and a hypertrophy and hyperplasia of the interstitial cells.—J. K.

THYMUS hyperplasia in children, Clinical study and treatment of—(Beiträge zur Klinik und Behändlung der Thymushyperplasie bei Kindern). Birh (W.), Monatschr. f. Kinderheilk., 1918, **14**, 363.

Birh reiterates the clear distinction between the symptom-complex of status lymphaticus and simple thymus hypertrophy. In the latter condition there is an isolated enlargement of the thymus dating back to fetal life, and here death comes from suffocation from pressure of the thymus on the trachea in a congenitally predisposed child; in such cases radiotherapy gives the best therapeutic results. In five cases reported by the writer there was rapid cure, from a clinical standpoint, with a gradual diminution of the gland itself as shown by radiographic examination. One of these cases showed a recurrence, but the others were followed to the fifth year of life, and showed a definite cure. The diagnosis of thymic hyperplasia is based upon a cardinal triad of symptoms; stridor, increased thymic dullness and radiographic evidence of enlargement. Other signs are attacks of asphyxia, dysphagia and, especially, lymphocytosis.—W. H. D.

Enlarged THYMUS gland in childhood. Brayton (H. W.), Proc. Connecticut M. Soc. (New Haven), 1918, **126**, 117-127.

This paper presents in a brief manner seven case reports in which enlarged thymus was diagnosed by x-ray examination. Three of the children died before radium therapy could be initiated; the remaining four responded satisfactorily to the treatment, and later x-ray pictures demonstrated reduction of the enlarged gland.—F. S. H.

(THYMUS) Thymic asthma in infants (L'asthme thymique chez les enfants). Exchaquet (L.), Rev. méd. de la Suisse Rom. (Geneva), 1918, **38**, 403-404.

E. considers that Paltauf's theory of the status thymo-lymphaticus is not supported by the facts and that from his own observations the mechanical action of a hyperplastic thymus is sufficient to explain the syndrome. He divides the cases into two categories: the one consists of individuals from 6 days to 14 months old, who are continually bothered with respiratory difficulties; the other group comprises those children in whom crises of suffocation occur while they apparently are in good health. Diagnosis is sometimes uncertain but can ordinarily be arrived at by exclusion. Radio-therapy lasting from two weeks to six months proved uniformly successful. The

report is followed by a brief discussion of thymus size and treatment.—F. S. H.

(THYMUS) Studies on acute leucemia. Lindblom (O.), Svenska. Läkaresällsk. Handl., 1919, **45,** 83-338.

It is of particular endocrine interest that the author found thymus alterations not only in the cases of lymphatic leucemia but also in several of the myeloid types. In 5 cases of the latter type myeloid inclusions, mainly of a perivascular type, were encountered.—J. A. H.

THYMUS, Changes in the—of children following different infectious diseases (Veränderungen der Thymusdrüse der Kinder bei verschiedenen Infektions-Krankheiten). Takeuchi (K.), Fukuoka-Ikwadaigaku-Zasshi, 1919, **12,** 25.

The author has made a study of the changes in the thymus gland in different infectious diseases, including "Ekiri," dysentery, simple enteritis, diphtheria, septicaemia, pneumonia and tuberculosis. Altogether he has collected 252 cases of which 162 were examined microscopically as well as macroscopically. He concludes that the chief changes are degenerative and destructive. He noted marked destruction of the so-called small thymus cells of the cortex and medulla, enlargement and phagocytosis of the reticulum cells of the cortex, and degenerative enlargement of the Hassall's corpuscles. In consequence of these regressive processes it is possible to recognize a primary increase and secondary atrophy of the parenchyma, an initial increase and subsequent decrease in the eosinophile cells, followed by an increase in the interstitial tissue. The regressive processes increase in proportion to the duration of the illness, reach a maximum between the 2nd and 4th days, and then gradually slacken. In the most acute infections, such as "Ekiri," dysentery and diphtheria, destruction is most apparent, while in the more chronic conditions there is more atrophy.
—E. V. C.

((THYROID) The causative factors of hematocele of the thyroid gland. Anon., Med. Rec. (N. Y.), 1919, **95,** 198-199.

The editor discusses the mechanism in formation of thyroid hematocele, and considers it comparable to a pelvic hematocele only that purulent transformation is much more frequent in the former.
—H. L.

(THYROID) The physiological action of the proteinogenous amines. III. The influence of the proteinogenous amines, phenyl-and p-oxyphenylethyl amine on the carbohydrate metabolism of the liver (Beiträge zur Kenntniss der physiologischen Wirkung der proteinogenen Amine. III. Über den Einfluss der proteinogenen Amine, Phenyl-und p-Oxyphenylethylamine auf den Kohlenhydratstoffwechsel der Leber). Abelin (J.), and Jaffee (I), Biochem. Ztschr. (Berlin), 1920, **102**, 39-57.

The subcutaneous injection and feeding of phenylethylamine and tyramine raise the catabolic processes of white rats and cause a lowering of the glycogen content of the liver. In view of the results on the gas exchange under similar conditions, it is concluded that this increased carbohydrate oxidation is related to a glycogen destruction in the liver. Since the injection of these amines and the feeding of the active substances of the thyroid lower the glycogen content of the liver and the animals remain alive, these compounds can be used to get this organ of the rat glycogen free.—F. S. H.

(THYROID) The physiological action of the proteinogenous amines. IV. Influence of di-iodo tyramine and tyramine on the development of frog larvae (Beiträge zur Kenntniss der physiologischen Wirkung der proteinogenen Amine. IV. Einfluss von Dijodtryamin und Tyramin auf die Entwicklung von Froschlarven). Abelin (J.), Biochem. Ztschr. (Berlin), 1920, **102**, 58-88.

Tyramine usually acts as accelerating agent for frog larva metamorphosis. This action is greatly increased if iodine is attached to the tyramine molecule, and is similar to that obtained when thyroid feeding is tried. The thyroid acts to increase disassimilation in that growth is retarded and metomorphosis accelerated. Di-iodotyramine gives this effect only on larva of a certain age, since young tadpoles are mainly inhibited in growth. Feeding with KI or iodo-lipoids had no accelerating effect on the metamorphosis of either young or older larva. Phenylethylamine in weak concentrations acts as a narcotic and shows itself to be a strong local anesthetic. [Cf. Swingle, Endocrin. **3**, 114-115.].—F. S. H.

(THYROID PARATHYROID) Strumipriva tetanie. Arnstein (A.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 224.

A demonstration of a woman of 54 years with sclerotic symptoms in muscles and connective tissues, who had a goiter

for 25 years. Four days after the removal of the goiter tetany developed in its classical form.—J. K.

(THYROID) Murillo's method for the evalution of antithyroid serum (Acerca del mitodo de Murillo para la valoracion del suero antitiroideo). Banus (J. S.), Siglo Méd. (Madrid), 1919, **66**, 668-671.

Murillo's method is based on the effects by which the antithyroid serum raises the resistance of guinea-pigs to the amount of diphtheria toxins necessary to produce death within twenty-four hours. Autopsy has shown the inhibition of the adrenal defensive mechanism. The author describes a series of experiments which showed the role played by the thyroid in the antitoxic defense against cocaine, which is taken as further proof in the confirmation of the defensive function of the gland. —E. B.

Vital THYROID-PARATHYROID activities. Ball (C. F.), Vermont Med. (Rutland), 1918, **3**, 17-20; 33-37.

A review—F. S. H.

(THYROID) Creatine and creatinine metabolism in myxoedema and the effect of the administration of thyroidin upon it (Kreatin-kreatininstoffwechsel bei Myxoedem und unter Einwirkung von Thyroidin). Beumer (Hans), & Tseke (C.), Berlin klin. Wchnschr., 1920, **57**, 178-179.

A patient of 13 years with myxoedema was treated with thyroidin and the creatinine metabolism studied. Large amounts of creatine were excreted but no changes were observed in the creatinine output. In normal individuals the same reaction is obtained after the administration of thyroidin, although it is less intense. The reaction in myxoedema may be explained on the basis of an increased destruction of proteins under the influence of the thyroidin.—J. K.

THYROID intoxication, Observations on—. Blackford (J. M.), Northwest Med. (Seattle), 1919, **18**, 199-201.

The author studied 74 exopthalmic goitre autopsies. All subjects under 40 years were found to have persistent thymuses of varying size. One-half of those over 40 had a large thymus and one-half no thymus at all. From these facts Blackford formulates the following deductions: 1, the thymus plays no causative role in exopthalmic goitre because half of the

older people died of that disease but had no thymus; 2, the thymus may exert a protective influence in exopthalmic goitre. These conclusions would be difficult to reconcile with the observations in cases of exopthalmic goitre which have been improved or cured by thymectomy. From a clinical standpoint, study of histories and autopsies suggest that if a patient with exopthalmic goitre lives one year after the inception of symptoms, he probably will not die from the disease before ten years have passed, and if then, usually from cardiac degeneration. No case of exopthalmic goitre showed active tuberculosis. No case of thyroid carcinoma was observed developing from exopthalmic goitre. About nine months after inception of symptoms most patients become suddenly very much worse. Operation at this time is accompanied by a very high mortality—25 per cent—and hence is contraindicated. Sometimes the patient without surgical treatment dies, but usually medical measures serve to tide them over this acute period. The author believes that x-ray, bromide, ergot, quinine, cold, etc., are of no benefit; that basal metabolism has been decreased only by rest and by operative reduction of the amount of functionating thyroid tissue. "In other words, exopthalmic goitre is a medical disease only until the patient is known to be in condition for operation; then operation should always be undertaken." [Many internists will disagree with the last pronouncement.] Many thymuses were found at autopsy in cases in which excellent stereoscopic x-ray pictures failed to reveal the gland,—even on review of plates after the autopsies. Thyrotoxic adenomata have been proven toxic by basal metabolism studies aside from clinical observation, and by striking improvement following operation, but they have no characteristic pathology. The author refers to the extraordinary power of Kendall's thyroxin in accelerating metabolism. He has shown that in heart block thyroxin will increase the ventricular rate, proving that it has a direct effect on cardiac tissue, and further emphasizing the relation of thyroid intoxication to cardiac degeneration.—H. L.

(THYROID) Blood picture in hyperthyreosis and goiter (Blutbefunde bei Hyperthyreose und Struma). Blank (G.), Deutsch. Arch. f. klin. Med. (Leipzig), 1920, **132**, 16-34.

The diagnosis of Graves' disease may be very simple, but in cases where certain characteristic symptoms are absent it may be extremely difficult. Kocher has reported that in Graves' disease the white corpuscles are diminished; that there is a neutrophil leucopenia with a relative or absolute lympho-

cytosis. Many authors have been unable to confirm these findings as typical of the disorder. Blank has carefully examined the blood in many cases of hyperthyreosis and goiter. He concludes that many contradictions in the literature may be explained as due to faulty diagnosis or bad technic in examining the blood. In Graves' disease the blood picture changes incessantly. In 30 per cent of the cases poikilocytosis was observed; in 50 per cent of such cases, and also of goiter, polychromatophilia was found. Basophilic stippling of the red corpuscles proved extremely common in both conditions seen in approximately 75 per cent. The number of blood platelets was diminished in 43 per cent of the classical cases of Graves' disease; in the formes frustes and in simple goiter this was never observed. In only 23 per cent of the classical cases of Graves' disease was the quantity of hemoglobin normal. In the others it was sometimes diminished, but is also often increased. In hyperthyreosis and in goiter the number of red corpuscles was normal. The color index in Graves' disease was sometimes high. It was found that neutrophilic leucopenia may be observed just as often in Graves' disease as in simple goiter. The number of eosinophilic leucocytes in both conditions was normal. Increase of the number of large mononuclear leucocytes was more frequently seen in the classical Graves' disease than in other diseases of the thyroid. In half the number of all diseases of the thyroid the number of lymphocytes was normal. In the remainder it was either increased or diminished. From these facts it may be concluded that the blood picture of Kocher has no diagnostic value in diseases of the thyroid.

—J. K.

(THYROID) Loss of flesh in women during the war (L'amaigressement des femmes au cours de la guerre). Blum (P.), Prog. Mèd. (Paris), 1918, **33**, 15.

Having eliminated from consideration those women whose loss of weight during the war was attributable to abnormal diet or tuberculosis, B. noticed that the greater number of those losing weight had the symptoms of thyroidism more or less complete. Four cases are reported as examples. The phenomenon is considered the effect and not the cause of the troubles, the causative factor in B.'s opinion lying in the sympathetic system.—F. S. H.

(THYROID) Basdowian psychosis (Psicosis basedowiana). Brabo (K.), Gac. med. Castellana, 1919, ——, ——.

A well studied case of hyperthyroidism accompanied by

mental confusion. The patient was much improved by antithyroid treatment.—E. B.

(THYROID) Cardio-thyroid syndromes (Sindromes cardio-tiroideos). Cañizo (A.), Siglo Médico (Madrid), 1919, **66,** 81, 130.

The author reports two cases of hyperthyroidism with the ordinary symptomatology of that disorder but with, in addition, predominating circulatory disturbances. The first patient had had a very light attack of "grippe." The second was a typical case of "Kropfherz." The patient had a persistent goiter which enlarged with each successive pregnancy, but diminished in the interim. She had had ten children. During the last pregnancy, following a great grief, the goiter, which had previously continued as the simple type, became hyperplastic, giving rise to the typical Graves' tetrad of symptoms. Only the cardiac conditions need be mentioned. By percussion and radiography, the cardiac area was found to extend to the sixth intercostal space, and laterally, to the mammillary line. Upon auscultation the tones in the mitral area were weak but in the aortic area somewhat resonant. The pulse,—100 beats per minute,—was small and compressible. There were irregularity and perpetual arrhythmia. In view of the fact that there was no history of antecedent infection or toxicosis, the author reasonably concludes that the cardiopathy is to be ascribed to the goiter.

In goiter two classes of cardiac disturbances are encountered, those due to the mechanical effects of the thyroid tumor and those due to thyrogenic toxins. Both Cañizo's cases were undoubtedly of the latter class. Various theories as to the mechanism whereby the cardiopathy is produced in such cases have been offered. Cañizo leans toward the idea that the continuous tachycardia with which the patients have to contend,—a condition which, in the hyperirritable state of the patients is readily evoked and continued by such causes as emotions, pregnancy, etc., keeps the muscle fibres over-active and without the normal rest period of ordinary diastole. This ultimately leads to nutritive failure and degeneration of the fibres, with consequent dilatation of the heart.—E. B.

THYROID activity, Some conditions affecting—. Cannon (W. B.) & Smith (P. E.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17,** 88-89.

See Endocrin, **4,** 386.

(THYROID) Two cases of interest in relation to the function of the thyroid. .Carmichael (F. A.), J. Kansas M. Soc. (Topeka), 1918, **18,** 83-85.

A report of two patients, each of whom showed a different degenerative process affecting the thyroid. The first was a case of calcareous degeneration of the thyroid in a cretin. On palpation the gland appeared slightly enlarged, somewhat indurated and irregular in outline. On removal the gland was found to weigh 105 grams and to contain numerous calcareous deposits varying in size from very small to that of a large bean. A rather complete histo-pathological report is given.

The second case was one of benign or slow-growing malignancy. No detailed description is given.—F. S. H.

THYROID, Surgical treatment of Exopthalmic Goitre. Crile (G. W.). Surg. Gynec. & Obst. (Chicago), 1920, **30,** 27.

Previously published in abstract. See Endocrin, **4,** 163.

(THYROID) Treatment of myxoedema by transplanting portions of a hyperplastic gland. Dowd (C. N.), Ann. Surg. (Phila.), 1920, **71,** 518.

The transplants were placed in the cancellous tissue of the head of the left tibia, in the preperitoneal tissue beneath the rectus abdominis, and in front of the rectus. Fifteen small punctures were made in other parts of the abdominal wall and little fragments of the gland were inserted. Marked improvement in the patient's condition is reported. After five months, dessicated thyroid was prescribed, however, as a precaution, for the patient's improvement was really remarkable.—J. F.

(THYROID-PARATHYROID) The influence of thyro-parathyroidectomy in the dog on the formation of natural antibodies and amount of heterohemolytic power of serum [Sur l'influence de la thyro-parathyroïdectomie (chez le chien); sur la formation d'anticorps naturels; dosage du pouvoir hétérohémolytique du serum]. Garibaldi (A.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 251-252.

In a former communication (See Endocrin **4,** 330), Garibaldi has shown that thyroidectomy favors the formation of immune antibodies in the rabbit. This raises the question of the regulatory role of the endocrine glands on the activity of the "antigenic organs." If this function exists, it is difficult to understand the results of Mlle. Fassin and Marbe, who found a diminution of natural heterohemolytic power after thy-

ro-parathyroidectomy, while Frouin obtained a contrary result. The present note records the author's observations upon the effect of thyro-parathyroidectomy on the natural heterohemolytic properties of dog serum. Protocols are given and the conclusion drawn that in the dog, thyro-parathyroidectomy increases the natural heterohemolytic power of the serum. The suggestion is made that the thyroids and parathyroids may play some role in blood regeneration. [See also Koopman, Endocrin. **3,** 318-320].—T. C. B.

(THYROID) Endemic goiter and cretinism in the high valleys of Alberche and Tormes (Sobre un foco de bocio y cretinismo endemico en los valles altos del Alberche y el Tormes). Goyanes, Siglo Méd. (Madrid), 1918, **65,** (2) 43; 85; 162; 182.

This is the first study of importance of the geographic distribution of endemic goiter and cretinism in Spain. Bircher supposed that these conditions arise only on lands that are marine sediments, and particularly on the marine deposits of the lands corresponding to the primary palaeozoic, triassic and tertiary periods. The observations of Goyanes in the valleys of Tormes and Alberche make possible the affirmation that formations of the archaiac group, granite, gneiss and crystalline deposits, are also sources of endemic struma. It is evident that water is one of the most important agents in the transmission of the supposed living cause of goiter. The theory that there are in the drinking water certain dissolved chemical substances such as calcium, magnesium, iron, etc., that determine the origin of endemic goiter is discredited. The studies of Marine and Lenhard and of Gaylor explain the appearance of endemic goiter on the basis of a living organism since they have observed in the affected regions the presence of hypertrophied thyroids in certain fish, as the trout. Goyanes could not find such conditions in the trout he studied. The experiments of McCarrison are cited, on the production of experimental goiter in man, and of its intestinal origin. A study of the dates in connection with the production of goiter seems to show that the water is not the only medium of contagion. The author's conclusions are as follows: Endemic goiter and cretinism appear to be diseases of infectious origin the source of which, however, is not known; cretinism is the result of a congenital hypofunctioning thyroid; it cannot be denied but must be affirmed that the transmission of the infectious agent from mother to child determines the congenital goiter and cretinism; sporadic goiter is also an infectious disease. Some infections produce thyroiditis similar to goiter (Chagas disease); the in-

fectious agent may invade the body through the bite of an insect; it is possible that the germ resides in the soil, by preference in those in which the organic material in decomposition is more abundant, but no statement can be definitely made that it is determined by any particular geological formation. It cannot be denied that water may be a medium of transmission and it is very probable that the endemic spreads by immediate contagion and mediation in the living; the strumous infection if not congenital at least appears very early in life; the intestinal localization of the organism is probable but not demonstrated.—E. B.

(THYROID) Some observations on goiter. Hawks (J. K. P.), Illinois M. J. (Chicago), 1918, **33,** 221-224.

An expression of the theory that the cause of the prevalence of goiter in the middle West is due to the drinking of the subterranean water of the glacial drift, which is analagous in its composition to the glacial waters of Switzerland, where goiter is so prevalent. Hawks considers that practically all goiters are surgical, and should receive early operative treatment.—F. S. H.

Reinforcing THYROID extract. Harrower (H. R.), South Calif. Pract. (Los Angeles), 1918, **33,** 39-40.

On the basis of the hypothesis that hypothyroidism means sub-oxidation: sub-oxidation means toxemia: toxemia means hypoalkalinity, and hypoalkalinity means demineralization, H. reinforces thyroid extract with a combination of salts closely following the salt composition of the blood. Treatment consists in giving 1/8 gr. to 1/2 gr. U. S. P. thyroid t. i. d. and 5 grs. of the salt mixture at the same time.—F. S. H.

THYROID function, Clinical results with a method of testing—. Harrower (H. R.), Med. Rec. (N. Y.), 1919, **96,** 722-725.

Reference again to the author's thyroid function test originally published in the Medical Record, August 3, 1918. This consists in the administration by mouth of four doses each 1/2, 1 and 2 grains of thyroid on three successive days, recording the pulse rate at regular intervals during this time, and noting symptoms such as irritability, twitching, breathlessness, etc. It is recommended by the author as a simple method of differentiating between hypo- and hyper-thyroidism. [The accuracy of such a test is open to question. A careful history and thor-

ough clinical examination would probably reveal more information, and if more precise studies were indicated, a Goetsch test or basal metabolism estimation would be preferred].—H. L.

THYROID hyperplasia and the relation of iodine to the hairless pig malady. I. Hart (E. B.) & Steenbock (H.), J. Biol. Chem. (Balt.), 1918, **33,** 313-323.

In an extended study of the hairless pig malady which occasions so much economic loss among the hog-raisers of Wisconsin, Hart and Steenbock have obtained evidence supporting the view that the disease is caused by a low iodine assimilation by either intestine or thyroid, resulting in a goitrous condition of both mother and young. This condition apparently interferes to a greater extent with the fetal development than with the normal maintenance of the mother.

When young sows are fed high-protein-level rations which have low laxative effects, and have accompanying conditions of lack of exercise and unclean surroundings, they are prone to develop thyroid enlargements. This is not so prevalent among the older sows. It is considered possible that some rations are so low in iodine as to make the scarcity of this element the direct cause. However, the authors state that the stage has not yet been reached when it is wise to advocate the general use of iodine in the feed of all brood-sows. But they do consider that in regions and on farms where hairless pig production is endemic or persistent in character the direct use of iodides should be made. [See also Smith, Endocrin. **3,** 262-272].—F. S. H.

Surgery of the THYROID. Haskins (J. B.), J. Tenn. State M. Ass. (Nashville), 1918, **11,** 91-96.

Of surgical interest, mainly.—F. S. H.

(THYROID) The question of iodine combination in the thyroid (Zur Frage der Jodbindung in der Schildrüse). Herzfeld (E.) & Klinger (R.), Biochem. Ztschr. (Berl.), 1919, **96,** 260-268.

When the tissue liquid is squeezed from pig thyroids and various iodine solutions are added thereto a certain amount of the element combines with substances in the extract. The results of these studies seem to indicate that the iodine in the thyroid is not only combined with the decomposition products of the protein surface, but is also in large part "built into" the cell protein. The authors conclude that these observations

speak against the conception that the iodine is an actual part of the thyroid secretion.—F. S. H.

(THYROID) Chemical studies of the physiology and pathology of the thyroid gland (Chemische Studien zur Physiologie und Pathologie der Schildrüse). Herzfeld (E.) & Klinger (R.), Münch. med. Wchnschr. (Munich), 1918-19, **65**, 647-651.

From the results of their studies on the effects of thyroidectomy the authors come to the conclusion that the thyroid secretion is not a protein complex, but is a dialysable split product. They consider that iodine is not an actual constituent of the secretion, but are of the opinion that its role is that of stimulating the formation of the secretion.—F. S. H.

(THYROID) Case of tertiary luetic thyroiditis accompanied by a high-grade laryngeal stenosis. Hœggström (A.) & Bergstrand (H.), Acta oto-laryngolog. (Stockholm), 1920, **2**, 207-237.

Hoarseness, air hunger, difficulty in swallowing, and cyanosis were present in a patient 41 years old. A tumor arising from the thyroid surrounded the larynx and trachea. Tracheotomy was performed on account of oedema of the glottis and suffocation. The Wassermann reaction was positive. Mercury treatment resulted in improvement, but this failed to last, and death ensued from suffocation about six months after the first appearance of the symptoms. Histological examination of the thyroid showed both interstitial and parenchymatous alterations. Each was a combination of gumma formation and interstitial chronic fibroplastic inflammation. A high grade of sympathetic involvement was also evident in the surrounding tissues. The parenchymatous alterations consisted in a proliferation of the thyroid follicles, which were entirely similar to those present in Basedow's disease. The panenchyma still present in traces in the gummatous necrosis was, however, of normal structure. This circumstance, taken with regard to the rest of the normal colloid, speaks for the idea that the proliferation of the follicles was of recent date, and a consequence of the action of the infectious agent.—J. A. H.

(THYROID) Goiter: Its early diagnosis and treatment. Holland (J. W.), Bull. Univ. Maryland School Med. (Balt.), 1918-19, **3**, 183-194.

A general presentation of the classification, causes, symptoms and treatment of goiter with clinical records of four cases, presenting no new data.—F. S. H.

(THYROID) Esophageal obstruction due to accessory thyroid. Hopkins (F. E.), Ann. Otol. Rhinol. & Laryngol. (St. Louis), 1918, **27,** 1258-1260.

Report of a case.—F. S. H.

THYROID response to overstrain. Hoxie (G. H.), Med. Herald (St. Joseph), 1920, **39,** 19-20.

The author cites the literature to show the tendency to consider thyroid hypertrophy as a reaction to adreninemia, to toxemia or to fatigue. He cites the experience of the troops in France as proof that the symptoms of hyperthyroidism may be simply such an attempt on the part of the body to maintain its chemical equilibrium. In brief, his experience was that soldiers came back to the base hospital after exhausting battles, with exposure to gas and infectious disease, showing a low blood pressure, dilated heart, and similar signs of exhaustion. The blood pressure would gradually rise until it reached 160 mm. With this increase in pressure was urinary urgency, tremor, heightened reflexes, and an increase in the size of the thyroid. In other words, in this stage the men presented the picture of Graves' disease.—Author's Abst.

(THYROID) Clinical data on goiter. Jones (E. G.), South. M. J. (Birmingham, Ala.), 1918, **11,** 682-685.

No new data.—F. S. H.

(THYROID) An unusual case of cretinism. Kerley (C. G.), Arch. Pediat. (N. Y.), 1919, **36,** 465-468.

This is the report of a case of a girl eight and a half years old, who displayed typical symptoms of cretinism when first seen by the author. Continual treatment for one year with thyroid extract 0.5-1.0 grain twice daily gave an increase of 6⅝ inches in height and of 8¾ pounds in weight, and also produced an appearance of normality. The case was reported because of the unusually good results obtained in one year's time, and despite its beginning at a relatively late age.

—M. B. G.

THYROID in uterine hemorrhage. Klass (O. C.), J. Oklahoma M. Ass. (Muskogee), 1918, **11,** 125-128.

A partial review of the literature and brief description of the favorable results obtained with personal cases of uterine hemorrhage by the use of thyroid extract. No details are given.—F. S. H.

(THYROID) Thyreohypoplasia congenita. Kasten, Med. Klin. (Berlin), 1918, **14**, 503; Deutsche med. Wchnschr., 1918, **44**, 559.

A demonstration of a 7-year-old girl presenting the classical symptoms of a hypoplastic thyroid.—F. S. H.

(THYROID) Acute strumitis (Akuten Entzündungen des Kropfes). Klose (Heinrich), Berlin. klin Wchnschr., 1920, **57**, 202.

A general review.—J. K.

(THYROID) Further course of the earlier described cases of retarded muscle contraction [Weiterer Verlauf der früher vorgestellten Fälle von verlangsamter Muskelkontraktion (Myxödem)]. Kramer, Berl. klin. Wchnschr., 1918, **55**, 989.

Three cases of retarded muscle activity were diagnosed as of hypothyroid etiology and thyroidin therapy initiated. The results in all three patients were good. There was increase in weight, decrease in lassitude, and a psychic rehabilitation. The muscular retardation has entirely disappeared and the reflexes have become normal.—F. S. H.

(THYROID) Myxoedema adultorum. Krisch (H.), Deutsche med. Wchnschr. (Leipz. & Berlin), 1918, **44**, 871.

Brief description and clinical findings of a case of myxoedema benefited by thyroid treatment.—F. S. H.

(THYROID) Local anaesthesia and technic of operations in goiter (Zur örtlicher Betäubung und Technik der Kropfoperationen). Kulenkampff (D.), Zentralb. f. Chir. (Leipzig), 1920, **46**, 246-249.

Of technical surgical interest.—J. K.

(THYROID ADRENALS) The influence of thyroid feeding upon carbohydrate metabolism. II. The epinephrine content of the adrenals of thyroid-fed rats. Kuriyama (S.), J. Biol. Chem. (Balt.), 1918, **33**, 207-213.

The epinephrine content of the adrenals of normal, medium sized rats is 2.2 mg. per gm. of the gland. In comparing this finding with the results of other investigators, the author decides that the epinephrine content of rat adrenal is the nearest to that of the dog, larger than that of the cat, and smaller than

that of sheep and calf. Thyroid feeding of either short duration with large doses or long duration with small doses does not materially change the epinephrine content, nor the weight of the adrenals of medium sized albino rats.

Kuriyama considers that if hypersecretion of the adrenals really exists in experimental hyperthyroidism, these results indicate that the excess of epinephrine is promptly transported into the circulation, the adrenaline content of the adrenals being kept fairly constant.—F. S. H.

THYROID, Cold abscess of the— (Abcès froid du corps thyroïde). Labey (M. G.), Bull. et mem. Soc. de chir. de Paris, 1918, **44**, 697-698.

Presentation of a specimen of abscessed thyroid removed from a goitrous woman. The diagnosis of tuberculous thyroid is given.—F. S. H.

THYROID in immunity, On the role of the—(A propos du rôle de la thyroïde dans l'immunitè). Launoy (L.) & Lévy-Bruhl, Compt. rend. Soc. de biol. (Paris), 1920, **83**, 90-91.

An answer to Garibaldi. (See Endocrin. 1920, **4**, 330.) In the author's experience thyroidectomy does not enhance the production of antibodies.—T. C. B.

(THYROID) A case of cretinism. Lennox (W. G.) & Read (B. E.), China M. J. (Shanghai), 1920, **34**, 140.

The case is that of a boy, 18 years old by Chinese count, who was admitted to the Peking Union Medical College Hospital, and who showed marked improvement on feeding six grains per day of dried thyroid gland.

The authors remark upon the fact that this is the only instance of cretinism which they have found in 35,000 cases treated at the dispensary, and that "perusal of a number of hospital reports from various parts of China fails to show record of cases of cretinism." This is the more remarkable since goiter is quite common in the vicinity of Peking and in other districts. They note, in addition, that the remarkable prevalence of goiter in some parts of China, and the fact that the Chinese are said to drink only hot tea, are inconsistent with the view that goiter is due to an infection caused by drinking unboiled water. The paper is accompanied by careful urine and water analyses.—E. V. C.

(THYROID) Graves' disease (Ueber die Basedowsche Erkrankung). Liek. Deutsche med. Wchnschr. (Berlin), 1920, **46,** 445-446.

The author observed 160 cases, including 100 of which the subjects were operated upon. There exists an intimate relation between the thyroid and brain. The "circulus vitiosus" in Graves' disease is: Increased secretion of the thyroid—increased irritability of the brain—increased secretion of the thyroid. Treatment may try to diminish the irritability of the brain or the hypersecretion of the thyroid. The first treatment, the internal one, is suitable for light cases only. The prime essential of this treatment is absolute psychical rest. The author is not convinced that x-ray treatment or milk of thyroidectomized goats has any therapeutic value. The best treatment attacks the thyroid surgically. The most important element is not the operative technique but the preparation of the patient. Before the operation he should be isolated and kept in bed for many days. The author advises ether anesthesia. The narcosis must begin and finish in bed, and not on the operation table. Of his 100 operated patients 3 died immediately after the operation; 2 died some time later of other diseases; 15 cannot be traced; 52 are cured; 20 are much better, and 8 are just the same as before the operation. Of these 8 cases, two underwent removal of the thymus; only in one case was any influence seen. In 3 other cases, after failure to benefit from thyroid extirpation, x-ray treatment of the ovaries was efficacious in curing the disorder.—J. K.

THYROID insufficiency after influenza (Dos casos hipotiroidismo post-grippal). López Albo (W.), Progresos de la Clinica (Madrid), 1919, **7,** 217-220.

The author gives the clinical histories of two children of 10 and 11 years, respectively, who, following an attack of influenza, developed extreme somnolency and headache. The fact that the cases improved under thyroid therapy is taken to indicate that they were due to hypothyroidism. They might, perhaps, be regarded as walking forms of encephalitis lethargica.
—E. B.

THYROID, A case of post-influenzal—hypo-function (Un nuevo caso de hipofuncion tiroidea post-grippal). Lopez Albo (W.), Prog. de la Clin. (Madrid), 1919, ——, ——.

Clinical history of a patient who presented the following conditions after having had a slight attack of the grippe:

paresthesia, general malaise, cephalagia, chills, cold extremities, lack of appetite, and edema of the eyelids. He was cured by thyroid therapy. The author is of the opinion that this case can be included among the thyroid disturbances of Lévi and Rothschild.—E. B.

(THYROID) Simple goiter—A public health problem. McCord (C. P.) & Walker (R. C.), Mod. Med. (Chicago), 1920, **2,** 124-132.

McCord and Walker have compiled all recent data with reference to the prevalence of simple goiter throughout the world, together with measures for the prevention of the occurrence of this disease. From the evidence available in these data they draw the following conclusions. The prevalence of simple goiter is common to many portions of this entire country. Inexpensive and readily applied measures have been devised for the eradication of this condition. These measures, although not yet fully standardized and simplified, have been demonstrated to be harmless and practicable. The school age coincides with the age of the highest incidence of goiter. The public and high school systems afford a splendid mechanism for carrying out these measures. It is believed that faithful application of these measures by public health workers, school and industrial physicians will go far in stamping out this widespread and distressing malady.—Author's Abst.

(THYROID) The surgical treatment of exophthalmic and thyrotoxic goiter with special reference to bilateral resection. MacLean (Neil J.), Surg. Gynec. & Obst. (Chicago), 1919, **29,** 475-480; Trans. West. Surg. Ass. (Minneapolis), 1919, **28,** 89-104.

The author points out the diversity of opinion between internist and surgeon in the treatment of exophthalmic goiter and the lack of unanimity as to operative indication and operative technique among surgeons themselves. It is stated that medical treatment in Graves' disease has not been satisfactory and the mortality and morbidity statistics of Sattler, Hector McKenzie, Kuttner and Hale White are quoted. While McCarrison says "there is no definite proof that the cures effected by surgical means are more lasting than those effected by medical means," Osler and Forchheimer are quoted as advocates of surgical treatment as both logical and scientific. The various surgical procedures are discussed, and the method of bilateral resection of the thyroid as advocated by Halstead was

the method adopted in the cases recorded, and had been the method used before the author heard Dr. Halstead's paper in Washington in 1913.

Emphasis is laid on the preparatory treatment for operation, especially having patience to wait until the wave of thyroid intoxication has well passed. By adopting this method the annoyance of preliminary ligation of vessels could in many cases be dispensed with and the complete operation of bilateral resection done in one stage. Emphasis is laid on the fact that exophthalmic goiter should never be considered a surgical emergency. The anaesthetic used in all cases was a combination of local anaesthetic (¼ of one per cent anocaine with adrenalin) and nitrous oxide with oxygen to induce unconsciousness. The operation consists in the low collar incision of Kocher and a flap of skin, superficial fascia and platysma dissected upwards. The infrahyoid muscles are separated in the mid-line and retraced laterally or, if necessary, divided transversely. Each lobe is then freed and dislocated from its bed. The superior thyroid vessels are first clamped and divided at the upper pole. Hemostats are now applied to the large veins as they course from before backwards on the surface of the gland. In applying these clamps the amount of gland to be preserved is borne in mind (usually one-sixth) and that above the clamps cut away. Bleeding from the cut surface is controlled by an over stitch. The remaining steps of the operation are completed in the usual manner with the exception that all veins in the flaps are underrun with fine catgut at some distance from the flap-edge, and tied so that no catgut comes in the line of incision. The platysma and skin are united by two separate silk worm gut sutures introduced subcutaneously. The resulting scar is almost invisible.

There are several advantages of bilateral resection over unilateral lobectomy or unilateral lobectomy with partial resection of the opposite lobe. Minimum injury is done to the parathyroids. Absolute safety for the recurrent laryngeal nerve is assured. If for any reason further removal of gland should be indicated, such as for recrudescence of symptoms of thyrotoxic activity, or the rare but possible occurrence of malignancy, the one side could now be completely removed with an assurance that some portion of gland remained. It is a physiological fact that where there are paired organs, should one be removed the other undergoes hypertrophy. This, while desirable in a condition where one is normal, is what we wish to avoid in the case under discussion, and this end is best obtained by double resection. Finally, for cosmetic purposes, in the operation of lobectomy there is a well marked depression

on the side from which the lobe has been removed, and on the other side the portion of gland left produces an undue prominence, while in bilateral resection the neck is obviously symmetrical.

In 31 cases in which the operation has been done there have been no fatalities.—Author's Abst.

(THYROID) Diagnosis and treatment of hyperthyroidism (Sobre el diagnostico y el tratamiento del bocio exoftalmico y de los estados hipertiroideos). Marañón (G.), Revista Ibero-Americana de Ciencias Médicas (Madrid), 1917, ——, —. (June.)

See Endocrin. **2,** 343.

(THYROID) Mongolismus mit Myxoedem. Moro, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 536.

A short note. A child presented typical mongoloid eyes, hyperflexibility, aplasia of the thyroid, dry hair, obstipation and idiocy.—J. K.

(THYROID) Osseous demineralization and its treatment (La deminéralization osseuse et son traitement). Robin (A.), Bull. gén. thèrap. (Paris), 1920, **171,** 61-74.

The loss of mineral substances from the bones is attributed to infectious diseases, such as tuberculosis and syphilis, dyspepsias accompanied by marked hyperchlorhydria, undernutrition, lowered alkalinity of the blood and lesions of the nervous system. The treatment consists in furnishing the organism an excess of the mineral salts it is losing, not in the pure form but as contained in foods rich in the necessary elements; in diminishing the ingestion of acid producing substances; and among other medications giving 2 mgm. of desiccated thyroid gland twice a day. Tables are given of the calcium and magnesium excretion of several individuals.—F. S. H.

(THYROID) Medical treatment of goiter. Ryan (G.), Med. Rec. (N. Y.), 1919, **96,** 534-536.

A brief, readable, conservative article, but presenting no new data.—H. L.

(THYROID) Curative versus symptomatic treatment of exophthalmic goitre. Sajous (C. E. de M.), Med. Rec. (N. Y.), 1919, **96,** 536-541.

A very interesting contribution leading to the conclusions that the symptomatic treatment of exophthalmic goiter generally resorted to compromises the chance of the patient's recovery, by leaving unassailed the primary cause of the disease. Many patients are subjected to thyroidectomy, entailing risks and morbid after-effects, who could be cured by medical treatment did the latter aim to remove the primary cause of the disease and its morbid effects. The remote results of surgical treatment would be greatly improved were removal of the primary cause of the disease and its morbid effects first insured. All cases of exophthalmic goiter are due primarily to some toxin originating from some pathological process in one or more organs, either the tonsils, sinuses, nose, nasopharynx, teeth or gums, stomach, intestines, genito-urinary organs, the nervous sytem, etc. Even the cases due to emotional stress have as their primary cause toxic wastes formed in the cerebrospinal neurons subjected to stress,—cholin, phosphoric acid, and particularly neurin, a highly poisonous waste product. These poisons, by exciting the thyroid apparatus to supranormal activity, owing to the active part taken by this apparatus in the defensive functions, cause it to excrete excessively, thus producing an additional toxicosis. The thyroid hormone, particularly when produced in excess, taking part also in tissue catabolism, breaks down fats, including the fatty bodies in nerves and brain cells, thus accounting for the striking nervous phenomena of the disease. Exophthalmic goiter thus becomes the product of a vicious circle in which three toxins take part: the primary causative poison which excites the thyroid; the excess of thyroid hormone as second poison; the excess of catabolic wastes due to the thyroid hormone, as third poison. Timely removal of the disorder which produces the primary causative poison, by arresting the excessive thyroid activity, will thus prevent the triple toxicosis, and cure the disease. The after-treatment, some such as described above, to insure cure, must also aim to remove the effects of the poisons. "Symptomatic treatment" should be dropped as an empiric method unworthy of modern science. —H. L.

(THYROID) A case of functional chorea with hyperthyroidism (Un caso de corea functional con hipertiroidismo). Sanz (F.), Real Acad. Nac. de Med. (Madrid), 1919, ——, ——, (Feb. 22).

The clinical history is as follows: mother neurotic, father normal; one sister presents symptoms of nervousness; personal antecedents unimportant; first menstruation at fourteen years at which time the first symptoms of the disorder appeared,

which have increased and consist of irregular movements that are brusque, incoordinated and involuntary, involving different parts of the body and many tics. During emotional stress they are augmented. Accompanying the chorea is a goiter and slight tremor; tachycardia is absent. The author considers it a case of hyperthyroidism but not of exophthalmic goiter, since the ocular symptoms are lacking. [In the opinion of the reviewer, the author attributes too much importance to the mere absence of exophthalmos. It is only one of many manifestations of hyperthyroidism and is by no means the most frequent.]—E. B.

THYROID function as influencing growth (Influencia de la function tiroidea sobre el crecimento). Sanz (L.), Aragon Méd., 1919, ——, —— (Feb.).

The results of this study lead the author to the conclusion that the thyroid secretion acts directly on growth in contradistinction to the other glands of internal secretion, which apparently act indirectly. The principal point of influence is osseous metabolism and the activle principle is a specific iodine containing compound. The thyroidal alterations are accompanied by changes in other glands of internal secretion, particularly the hypophysis and gonads, which also add their quota to the growth processes. The climatic influence on growth is exercised through its modifying effect on the thyroid. All diseases which alter the nature of growth produce disturbances in the thyroid functions.—E. B.

(THYROID) Metabolism, report of a case. Schwartz (C. W.), Am. J. Roentgenol. (Detroit), 1920, **7**, 229.

A preliminary report on the case of a young man, twenty-seven years of age, who came to the hospital because of extreme nervousness and restlessness. He presented upon examination an enlarged thyroid gland, a loud bruit, tachycardia, exophthalmos, lid lag, tremors of the hands, sweating, and Hutchinsonian teeth, together with a positive Wassermann test and a markedly increased metabolic rate. In the course of three months, by means of a series of x-ray treatments, the technical details of which are given by the author, the rate was lowered 67 points.—J. F.

(THYROID) Aetiologie des Mongolismus. Stölzner, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 200.

The mothers of mongoloid children are often rather old or worn out by many confinements. In three cases observed by

Stölzner, the mother showed hypothyroidism. The author advises the administration of thyroid during pregnancy.

Homoplastic THYROID transplants. Swingle (W. W.), Anat. Rec. (Phila.), 1920, **18,** 263.

Experimental evidence is presented in support of the author's hypothesis that the long period of larval life of certain species of anurans (Rana catesbiana, for example) is due to the slow rate of thyroid development. Grafting the thyroid glands of advanced second-year tadpoles into small, immature first-year tadpoles produced rapid growth in the latter up to the stage of development shown by the animals from which the glands were obtained.—W. J. A.

(THYROID) A study of the distribution of iodine between cells and colloid in the thyroid gland. I. Methods and results of study of beef, sheep, and pig thyroid. Tatum (A. L.), J. Biol. Chem. (Balt.), 1920, **42,** 47-54.

When frozen section preparations of unfixed thyroid glands are floated in isotonic salt solutions the colloid separates out. Using this phenomenon as a basis of procedure Tatum prepared large amounts of sectioned material from relatively fresh glands and extracted with Ringer's solution and centrifuged. This was repeated and iodine determinations were made on the residual cell bodies, the whole glands and the extracts. There appeared to be a wide variation in the absolute amounts of the total iodine in the whole glands and cell masses. Nevertheless, the ratio of the percentage of iodine in the cells to the percentage of iodine in the whole gland was found to be a fairly constant value, and was considerably less than 40 per cent. From these results it is evident that iodine exists in both the cells and the colloid of beef, sheep and pig thyroid glands.—F. S. H.

(THYROID PARATHYROID) Tetanie-epilepsie. Tilling. Deutsche med. Wchnschr. (Berlin), 1920, **46,** 200.

There exists a close relationship between tetany and epilepsy. The author treated two cases with thyroidin (3 times daily with 1 gram) as indicated by Bolton and with parathyroidin (Freund and Redlich) without result.—J. K.

(THYROID) Diagnosis of Basedow's disease. Troell (A.), Hygiea (Stockholm), 1920, **82,** 33-45.

Goetsch's adrenalin diagnosis test was carried out on 6 Basedowians and 4 uncomplicated goiter cases with entirely satisfactory results.—J. A. H.

(THYROID HYPOPHYSIS OVARY) Remarks on the cure of various forms of headache and "faceache" by electrical methods. Hernaman-Johnson (F.), Practitioner (Lond.), 1919, **103,** 297-305.

As far as the ductless glands are concerned, the author refers to headache as a frequent symptom in exopthalmic goitre which disappears under suitable x-ray treatment. Disease of the pituitary gland may cause headache of a very terrible kind. A few cases, he says, are on record in which x-ray treatment of pituitary gland enlargement has produced benefit. He believes menstrual headaches to be due to ovarian hypersecretion and maintains that such headaches yield to x-ray treatment given with a view to reducing ovarian activity.

—H. L.

(THYROID) Changes in the larynx and trachea in benign goiter (Veränderung des Larynx und der Trachea bei gutartiger Struma). Wodak, Münch. med. Wchnschr. (Munich), 1919, **66,** 1365; Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1400; Wien. klin. Wchnschr. (Vienna), 1920, **33,** 73.

In many cases of benign goiter there may be seen in the larynx and trachea changes of the nature of displacements, compression, distortions, catarrh of the mucous membranes and paralysis of the recurrent laryngeal nerve. The distortion is rarely described, but frequently occurs.—J. K.

(THYROID) A mentally deficient child with a protracted elevation of temperature. Wolf (G. D.), Med. Rec. (N. Y.), 1919, **96,** 880-883.

Report of a case presenting difficult problems of differential diagnosis, much improved by administration of thyroid.

—H. L.

THYROID and PARATHYROID tumors of the tongue. Wood (F. C.), Proc. N. York Path. Soc. (N. Y.), 1916, **16,** 84-89.

Wood describes briefly three cases of thyroid tissue masses occurring at the base of the tongue, in two of which were found small areas resembling parathyroid tissue. A brief reference is also made to other such cases reported in the literature.

These aberrant masses usually occur in the median iine or near it at the base of the tongue. It is suggested that parathyroid tissue may in such cases as these arise from the second branchial pouches, as well as from the third and fourth, as normally.

I. M.

TISSUE EXTRACTS, Action of—upon coagulation of blood. Uchihara (K.), Taiwan Igakukai Zasshi, 1918, No. 182, 119-130.

The author isolated a globulin from extracts of different organs, and found that it accelerated the clotting of blood. He also isolated a nondialyzable albumin-like substance which hindered blood coagulation. This substance was always present in the same amount, while the amount of the globulin was variable. (Abstract in China Med. Jour.)—L. G. K.

(THYROID) Basedowism in a syphilitic family. Zeleneff (I. F.), Russk. J. Kozhn. i. Ven. Bolizen (Mosk.), 1916, **31**, 19-24.

In the cases studied Basedowism developed after infection with syphilis. Antisyphilitic treatment diminished the symptoms of Basedowism. Z. concludes, therefore, that the poison of syphilis has an etiological relationship to the symptoms of Basedowism.—S. H.

The abstracts in this number have been prepared by the staff, assisted by:

E. Bonilla, Madrid, Spain.
W. H. Donnelly, Brooklyn, N. Y.
Samuel Hanson, San Francisco.
L. G. Kilborn, University of Toronto.
Irvine McQuarrie, Baltimore.

With the permission of the editors, certain abstracts have been quoted from "Physiological Abstracts," "Chemical Abstracts" and "Surgery, Gynecology and Obstetrics."